Volume 49 *Number* 2

SURGERY

FEBRUARY, 1961

Original communications

Tumor size, duration of symptoms, and prognosis in carcinoma of the breast

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The size of a breast tumor at operation and the duration of its symptoms prior to operation are readily available from most patients' histories. Prognostic value of these facts is at present obscured by contradictory reports. A number of authors[1, 3, 4, 14] have described a correlation between tumor size and death, while others[6, 8, 9] have concluded that there is little or no such relationship. There is even more disagreement with respect to duration of symptoms. Hoopes and McGraw[6] and Haagensen and Stout[3] have stated that there is a decrease in survival rate with longer duration of symptoms, the differences they report do not seem to be statistically significant. Kunath[9] and Hawkins[5] state that there is little or no correlation between duration of symptoms and death, but neither give supporting figures. Nathanson and Welch[12] found that patients with the shortest delay in receiving treatment have the worst prognosis, but they also gave no figures. A third group[1, 11] report a decline in survival with increasing duration of symptoms up until 1 or 2 years, after which the survival rate again rises.

We have attempted to relate these factors to each other, to the age of the patient, and to the prognosis of the disease.

Received for publication June 10, 1960.

MATERIAL

From a series of 357 cases of breast cancer among white patients in a private hospital operated upon in Atlanta between 1925 and 1954,[13] we have selected 289 patients for whom time of onset was adequately recorded. All but 3 were diagnosed as having adenocarcinoma. We are aware that the time of the discovery of a breast tumor reported by the patient depends upon her alertness and her subsequent memory and veracity with regard to the discovery.

Table I. *Tumor size and time from discovery to operation (223 patients)*

Time from discovery by patient to operation	*Tumor size at operation*					
	Under 2 cm.		*2.0 to 3.9 cm.*		*4.0 cm. or over*	
	No.	*%*	*No.*	*%*	*No.*	*%*
1 month or less	20	45.5	41	41.4	32	40.0
Over 1 month, under 1 year	22	50.0	43	43.5	31	38.8
1 year or over	2	4.5	15	15.1	17	21.2
Totals	44	100.0	99	100.0	80	100.0

Lewison[10] has emphasized the dangers in basing conclusions upon such information. To minimize error we were content to know that the tumor had been recognized prior to operation for (1) 1 month or less, (2) over 1 month but less than 1 year, or (3) 1 year or more. Closer timing of onset probably decreases reliability without gain in information.

Tumor size was taken from the pathologist's report, not the clinical report.

RESULTS

Table I shows the distribution of size of tumors at operation by their preoperative duration. As might be expected, few tumors of the smallest size had been evident for over 1 year. It is perhaps a measure of the alertness of our patients that among 223 tumors, 44, or one-fifth, were detected early enough that they were still under 2 cm. in diameter at the time of removal. They constituted 21.5 per cent of those said to have existed for 1 month or less before operation and 5.9 per cent of those said to have been present for 1 year or more. Ninety-three (41.7 per cent) in all size classes were operated upon within 1 month after discovery. The tumors most frequently found at operation were in the 2.0 to 3.9 cm. size range (44.4 per cent).

Of the 32 largest tumors said to have existed for 1 month or less, 12 proved fatal in less than 5 years. There is no way of knowing whether such tumors grew extremely rapidly or whether the patients represent a less observant group.

When the incidence by size at operation was considered from the standpoint of whether the patients were under or over 50 years of age, a few more smaller and a few less larger tumors were found among the older patients (Table II). The difference is not statistically significant for the number of cases available, although we suspect that it might prove to be so in a larger series. This is in agreement with a slight decrease in postmenopausal mortality rate and a better 5-year survival rate (62.5 per cent compared with 51.0 per cent among women under age 50) found among the older patients in our earlier study.[13]

When we consider the time between discovery of the tumor and operation in the older women, there is a marked difference. Twice as many women under age 50 wait for 1 year or more before seeking help than do older women, and over half the women operated upon within the first month are in the older group. It is probable that fear of mutilation weighs less heavily upon postmenopausal women than does the fear of death, in comparison with women still in the childbearing age. They are hence less prone to procrastinate. The greater likelihood that a swelling in the younger women may prove to be a benign mastitis perhaps also contributes to the delay in operative treatment (Table III).

Table II. *Patient's age and tumor size at operation (234 patients)*

Age	*Tumor under 4 cm.*		*Tumor 4 cm. or over*	
	No.	*%*	*No.*	*%*
20-49 years	72	47.7	44	53.0
50-89 years	79	52.3	39	47.0
Totals	151	100.0	83	100.0

LOCATION

Tumors are more common in the upper half of the breast among patients in this series. There were 165 in the upper and 67 in the lower half. There was a slight tenddency, probably not significant, for those in the lower half to be smaller at time of operation (Table IV).

Although the size difference was not marked, tumors in the lower half of the breast resulted in earlier operation than did those in the upper half. Very few of the former were permitted to persist for 1 year or more (Table V).

As the difference between the time elapsing from discovery to operation is greater than is accounted for by the difference of tumor size at operation (Table IV), we must conclude that tumors in the lower half of the breast produce more discomfort (perhaps from the pressure of brassieres) and hence cause the patient to seek attention earlier, or else we must assume that such tumors have intrinsically faster growth than those of the upper half. The greater mortality rate from tumors in the lower half of the breast may strengthen the latter view. No such differences in time of discovery were found when medial or lateral halves of the breast were compared. There was no difference between the pattern of the left and right breasts.

Thirty-four of the 52 patients with tumors 4 cm. or larger at operation died within 5 years after their operation, while only 28 out of 83 of those with smaller tumors died. Five-year survival rate was thus 34.6 per cent for those with large tumors and 66.3 per cent for those with small tumors at operation. Half of the patients with tumors under 2 cm. in diameter were free from disease 5 years after operation, while about one-fifth of those with tumors of large size were in this group. Frequency of large and small tumors by 5-year survival is shown in Tables VI and VII.

The tendency toward earlier discovery of large tumors is more marked among the patients who eventually lived for 5 years or more after operation than among the shorter-lived patients. We have shown in an earlier paper[13] that operative delay resulted in only a very slightly shortened survival time and that the observed difference is of low statistical significance ($p < 0.10$ or 1 chance in 10 that the difference is accidental). When only the 5-year survival time is considered the significance falls to a 50:50 chance that the difference is accidental (Table VIII and Fig. 1).

Table III. *Patient's age and time from discovery to operation (289 patients)*

Time from discovery by patient to operation	*Patients under 50 years*		*Patients 50 or older*	
	No.	*%*	*No.*	*%*
1 month or less*	52	35.6	66	46.1
Over 1 month, under 1 year	70	48.0	65	45.5
1 year and over*	24	16.4	12	8.4
Totals	146	100.0	143	100.0

*Between the first and third groups $\chi^2 = 5.636$, $p < 0.02$.

Table IV. *Location and size of breast tumors (252 patients)*

	Total		*Tumor under 4 cm.*		*Tumor 4 cm. or over*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Upper half	165	100.0	105	63.6	60	36.4
Lower half	67	100.0	48	71.7	19	28.3

$\chi^2 = 1.362$, $p < 0.25$.

Table V. *Location of breast tumors and time from discovery to operation (196 patients)*

Time from discovery by patient to operation	*Tumor in upper half of breast*		*Tumor in lower half of breast*	
	No.	*%*	*No.*	*%*
1 month or less*	57	38.5	26	54.2
Over 1 month, under 1 year	71	48.0	21	43.7
1 year and over*	20	13.5	1	2.1
Totals	148	100.0	48	100.0

*Between the first and third groups, $\chi^2 = 6.152$, $p < 0.02$.

Table VI. *Size of breast tumor and 5-year survival (135 patients)*

	Size of tumor					
	Under 2 cm.	*2.0-3.9 cm.*	*4.0-5.9 cm.*	*6.0-7.9 cm.*	*8 cm. and over*	*Total*
Died of cancer, under 5 years	5	23	22	8	4	62
Alive 5 years, not free of disease	7	24	5	3	1	40
Alive 5 years, free of disease	12	12	9	0	0	33

Table VII. *Summary of Table VI*

	Under 4 cm.		*4 cm. or over*		*Total*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Lived less than 5 years	28	45.2	34	54.8	62	100.0
Alive 5 years or more	55	75.3	18	24.7	73	100.0

$\chi^2 = 12.896$, $p < 0.001$.

Time elapsing from discovery to operation was less important, however, than was the size the tumor had reached at the time of operation in the same group of patients. Of women surviving operation for 5 years or more, three-fourths had tumors less than 4 cm. in diameter. Of those who died sooner, fewer than half had tumors so small (Fig. 2). The probability that this difference is due to chance is only 1 in 1,000 ($p < 0.001$).

None of the 33 patients considered free from disease 5 years after operation had had a tumor 6 cm. or larger in diameter at the time of operation, whereas 12 out of the 62 patients who died of cancer within 5 years had had tumors in this size range.

Among 72 patients known to have died of cancer, 36, or 50.0 per cent, had had tumors of less than 4 cm. in diameter at operation. Of this group, 9, or 25.0 per cent, were alive 5 years after operation. Among the 36 with tumors 4 cm. or larger at operation, only 2, or 5.6 per cent, lived this long (Fig. 3).

Thus, even when the patient is doomed to die of her disease eventually, the size of the tumor at operation is still related to her life expectancy.

It will be noticed from Fig. 3 that the major difference between the two survival curves lies in the mortality rate during the *first postoperative year,* and that subsequently the rate of death is similar, as evidenced by the parallel curves. The mean life expectancy of the group with the larger tumors at operation was about 16 months, while for those with the smaller tumors it was 36 months. If eventual death from cancer implies that foci of malignant cells have been left in the body after operation, this graph implies that such foci left from smaller tumors are fewer or grow less rapidly, at least during the first postoperative year, than do similar foci from larger tumors.

The difference in age distribution (Table II) between the two groups can not account for the difference in mortality rate, as only patients who died of their disease are included. That slightly more of the smaller tumors were in older women is reflected in the slightly lower mortality rate previously[13] observed in the 50 to 59 year age group.

Table VIII. *Average survival and time from discovery to operation (82 patients)*

Time from discovery to operation	*No. of cases*	*Average survival time (mo.)*
1 month or less	36	40.3
Over 1 month, under 1 year	30	31.7
1 year or more	16	34.0

Coefficient of correlation, $r = 0.069$.

DISCUSSION

As a breast tumor may be assumed to start from one or a few cells, it should be evident that increasing size and increasing delay in treatment represent progress of the disease. There has been little agreement, however, as to the prognostic value of these two factors.

Kreyberg[7] has discussed the expression "early diagnosis" and its several meanings in clinical use. A tumor may be said to be diagnosed early (1) while still in stage I, (2) when the time from the first symptom is short, or (3) when the tumor is of the smallest detectable size.

When the first definition is used, failure of cure represents only a mistake of staging. When the third definition is used, Kreyberg and Christiansen's[8] results indicate that two-thirds of their patients' tumors had metastasized even while very small. In their data only 6 per cent were smaller than a hazelnut (approximately 2 cm.) at operation.

Our experience has been better than this. Twenty-four out of 135 (17.8 per cent) patients had tumors less than 2 cm. in diameter at operation. Of these, 12 were free from disease after 5 years, 7 were alive but not free from disease, and 5 had died of cancer. In spite of these differences, the data from the present series lends little more support to the idea of a close relation between size and duration of symptoms than does that of Kreyberg and Christiansen[8] (Table I). Agreement is better among women over age 50 than among younger ones. We must agree with Haagensen[2] that there is only a trend toward an increased frequency of the smaller tumors among the patients who have had symptoms for the shortest length of time.

Duration of symptoms does not correlate well with size of the tumor at operation or with subsequent survival time. To what extent this may be due to poor patient memory rather than to the nature of the disease is not clear. We believe that it is largely due to variations in rates of tumor growth.

Size of the tumor is of considerably greater value in prognosis with respect to

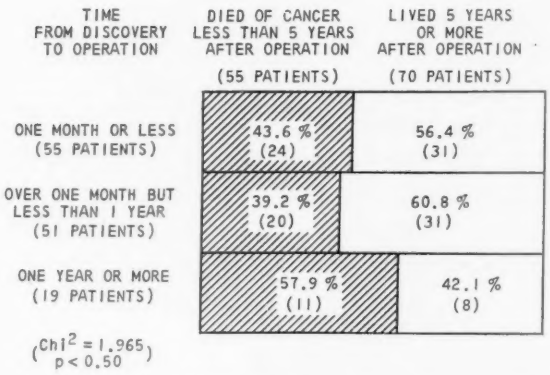
TIME FROM DISCOVERY TO OPERATION
DIED OF CANCER LESS THAN 5 YEARS AFTER OPERATION (55 PATIENTS)
LIVED 5 YEARS OR MORE AFTER OPERATION (70 PATIENTS)
ONE MONTH OR LESS (55 PATIENTS)
43.6 % (24)
56.4 % (31)
OVER ONE MONTH BUT LESS THAN 1 YEAR (51 PATIENTS)
39.2 % (20)
60.8 % (31)
ONE YEAR OR MORE (19 PATIENTS)
57.9 % (11)
42.1 % (8)
(Chi² = 1.965, p < 0.50)

Fig. 1. Relation between time from discovery of tumor to operation and 5-year survival in 125 breast tumor patients.

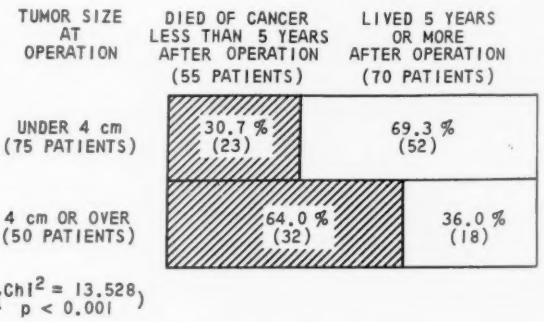
TUMOR SIZE AT OPERATION
DIED OF CANCER LESS THAN 5 YEARS AFTER OPERATION (55 PATIENTS)
LIVED 5 YEARS OR MORE AFTER OPERATION (70 PATIENTS)
UNDER 4 cm (75 PATIENTS)
30.7 % (23)
69.3 % (52)
4 cm OR OVER (50 PATIENTS)
64.0 % (32)
36.0 % (18)
(Chi² = 13.528, p < 0.001)

Fig. 2. Relation between size of tumor at operation and 5-year survival in the same 125 breast tumor patients as in Fig. 1.

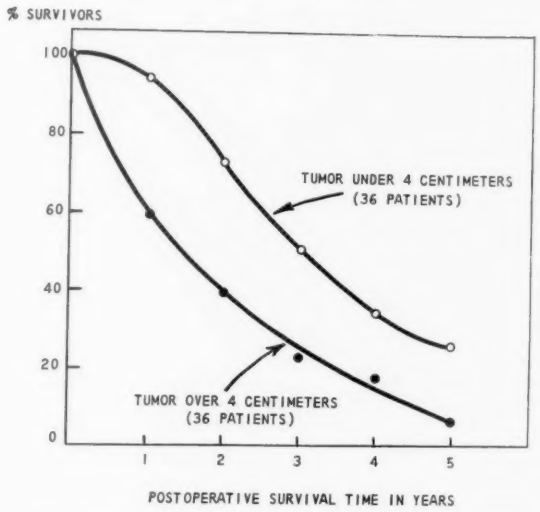

Fig. 3. Survival rate and size of tumor at operation in 72 patients who eventually died of cancer

subsequent freedom from disease and to survival time even when death from cancer eventually occurs. The prognosis for subsequent freedom is about twice as good for patients with tumors of less than 4 cm. Even for patients not free of their disease, the 5-year survival rate is 4 times as great for those with smaller tumors at operation.

SUMMARY

1. Size of breast tumor and duration of symptoms among 289 patients has been related to age, survival, and prognosis.

2. About 40 per cent of tumors regardless of size had been discovered within 1 month prior to operation. Fewer than 5 per cent of those under 2 cm. in diameter had persisted for 1 year or more.

3. Older patients sought treatment more promptly after the discovery of a tumor than did younger patients. Their tumors tended to be smaller and their survival time longer, although the differences are not statistically significant.

4. Tumors in the lower half of the breast tended to be smaller at operation and were treated more promptly after their discovery by the patient than were tumors in the upper half. No such difference occurred between the medial and lateral halves.

5. Patients who died of cancer within 5 years after operation had a significantly larger percentage of tumors over 4 cm. in diameter at operation than did patients who lived for more than 5 years. No patient free from disease 5 years after operation had a tumor over 6 cm. in diameter.

6. Among patients in this series who are known to have died of cancer, survival was from 18 to 24 months longer when the tumor was less than 4 cm. in diameter at operation than when it was larger. Five-year survival rates of the patients with the smaller tumors was 25.0 per cent and with larger ones 5.9 per cent.

7. Size of the tumor at operation appears to be of much greater prognostic value than duration of the tumor prior to operation.

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Surgical aspects of infrapapillary duodenal tumors

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Primary duodenal tumors remain extremely uncommon, and the majority of those encountered take their origin from the tissue in the general region of the duodenal papilla. The rarity of tumors of the duodenum located distal to the papilla renders information concerning them rather meager. Since no sizable series have been reported, the majority of the articles are concerned with details of isolated cases or collective reviews of the literature. Many of these reports have included only short-term follow-up studies.

For the purposes of definition, the present discussion will be confined to tumors of that part of the duodenum beginning at the distal aspect of the second, or descending, portion immediately distal to that point which receives the termination of the common bile duct and the pancreatic duct, and ending where the intestine turns abruptly forward to become the jejunum at the duodenojejunal flexure, which is held in place by the ligament of Treitz. This restricted portion of the intestinal tract may be relatively inaccessible for surgical exposure. Of greater importance is the fact that tumors in this small area may present symptoms that are difficult to differentiate from those of other more common lesions in the upper part of the abdomen. The gravity of this peculiar circumstance is obvious when one notes the extensive growth achieved by some of these tumors before the symptoms lead to surgical intervention, which finally is undertaken long after the "golden opportunity" for curative resection has passed.

It was thought that a review of a series of cases of primary infrapapillary duodenal tumors studied at a single institution and possessing a significant follow-up survey would be worth while.

BACKGROUND INFORMATION

Benign duodenal tumors have not seemed so extremely rare to the surgeon because certain types of them are easily seen in the first and second portions of the duodenum. However, infrapapillary benign lesions are extremely uncommon from the surgical standpoint. Cole[3] presented a summary of reports in the literature up to 1953 and included all types of benign duodenal tumors. He classified as fibromyomas all lesions reported as having any myomatous elements, such as myomas, fibromyomas, or leiomyomas, since they all contain smooth muscle and fibrous tissue. His survey disclosed that adenomas, fibromyomas, and pancreatic rests make up almost three-fourths of benign duodenal lesions. As one would expect, aberrant pancreatic tissue is relatively common, and an occasional hemangioma is encountered. Cole did not classify the benign

Abridgment of thesis submitted by Dr. Higgins to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

Received for publication June 15, 1960.

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lesions with respect to the portion of the duodenum most commonly affected.

With regard to symptoms, 13 of the 17 benign tumors in the series of Joergenson and associates[12] were entirely asymptomatic, which is in complete accord with most of the published reports. Hemorrhage appears to be the most common symptom of the benign lesions, according to Balfour and Henderson.[1] It is more common in association with tumors of muscular origin than with other types of benign lesions, according to Briggs and Roberts.[2] Melena is mentioned frequently, and most authors emphasize that the possibility of benign tumors of the small intestine always should be considered in the presence of hemorrhage from the upper part of the gastrointestinal tract when there is no evidence of peptic ulcer or gastric tumor. Here again, restriction of these tumors to the infrapapillary portion of the duodenum has not been the rule in previous reports. Pain of an ulcerlike nature is said to be a feature if erosion of the tumor is present, and nausea and vomiting may be prominent if the tumor is of sufficient size. Hoffman and Grayzel[9] stressed these symptoms. Rankin and Newell[17] reported that the average duration of symptoms before surgical intervention in the benign lesion is about 8 years and that the average age of the patients is 41.6 years, or almost 15 years less than that of a comparable group with malignant duodenal tumors.

The majority of authors are of the opinion that the diagnosis of these lesions may be made rather accurately by an experienced roentgenologist. The benign growth is said to present a thick, rounded, oval, or lobulated filling defect with clear-cut outlines within the duodenal lumen. If roentgenologic examination shows the growth to be smooth and mobile and without evidence of infiltration of the duodenal wall, it would appear most likely that the lesion is benign. The presence of a pedicle apparently also favors the roentgenologic diagnosis of a benign tumor.

Primary carcinoma of the duodenum apparently is an extremely rare lesion. Eger[8] reviewed the records in 350,286 necropsies and found only 126 cases of primary duodenal carcinoma, an incidence of 0.033 per cent. Only 12 per cent of these lesions were distal to the papilla. Howard,[11] in a collected series of 117,433 necropsies, reported the incidence to be 0.045 per cent; 37 per cent of carcinomas of the small intestine were in the duodenum. Mayo[14] found that 29 of 108 malignant tumors of the small intestine were in the duodenum.

Sarcoma of the duodenum is an even rarer lesion. Carcinoma predominates over sarcoma in this location in a ratio of about 10 to 1, as opposed to the remainder of the small intestine, where sarcoma is a relatively more frequent lesion. The greatest number of primary malignant tumors of the duodenum are reported to involve the second, or peripapillary, portion and this is undoubtedly due to the fact that many carcinomas of the ampulla of Vater may well have been included in the group. Dixon and co-workers[5] stated that, if ampullary carcinoma is excluded, the incidence of carcinoma in the various portions of the duodenum is approximately equal.

Copeland and Greiner,[4] and also Weinstein and Roberts,[20] reported that lymphosarcoma and leiomyosarcoma are the commonest sarcomatous lesions of the duodenum. Weinstein and Roberts summarized the literature up to 1953 and found reports of only 27 cases of duodenal leiomyosarcoma. Eleven of these lesions involved the infrapapillary portion.

Hoffman and Pack[10] stated that primary carcinoma of the duodenum is extremely rare in patients under the age of 40 years. They found that most of these lesions occur in the fifth and sixth decade of life, the average age being from 52 to 55 years. The lesions are said to predominate in men over women in the ratio of 3 to 1. With regard to infrapapillary duodenal carcinomas, Duff and associates,[6] as well as Odelberg,[15] reported that the age and sex incidence is the same as that for carcinoma of the duodenum in general. Weinstein and Roberts noted that leiomyosarcoma may occur from the

fourth to the seventh decades of life, with an equal sex incidence. Copeland and Greiner stated that lymphosarcoma occurred 3 times as often in men as in women, with a peak incidence in the first, third, and fourth decades.

Pathologic studies of the specimens reported showed that adenocarcinoma is the commonest tumor in the infrapapillary portion of the duodenum. Carcinoids located in this zone also have been reported. Duff's group, and also Hoffman and Pack, divided adenocarcinoma of the duodenum into 3 types according to the gross appearance. The first type is the scirrhous, or annular, tumor which leads to constriction with obstruction. This tumor is characterized histologically by overproduction of fibrous tissue. The second gross category is the polypoid, with intraluminal projections that tend to ulcerate and bleed. If the growth is extensive enough, obstruction is produced. The third gross type is "colloid" carcinoma. Microscopically, this tumor presents cystic spaces filled with mucus and signet-ring cells.

Prey and associates[16] stated that sarcomas arise in the submucous and muscular layers of the duodenum and tend to grow longitudinally, infiltrating the wall. They are usually hard or elastic neoplasms that develop more slowly than do carcinomas and tend to remain better delineated. They usually do not metastasize early. When they do spread, it is usually by way of the blood stream. Leiomyosarcomas are especially prone to ulcerate and undergo central necrosis.

From a study of the collected reviews, it is apparent that the symptoms of malignant tumors of the infrapapillary portion of the duodenum are nonspecific and present no characteristic clinical syndrome. It is usually difficult to make the diagnosis unless a high index of suspicion is maintained. Dixon's group[5] thought that the clinical features depended more on the type and the state of advance of the growth than on its position within the duodenum. A strikingly important clinical feature is the complete absence of jaundice, since the infrapapillary lesions do not approach the ampulla. It is obvious that obstruction of the duodenum finally will lead to the diagnosis if the extent of the tumor is great enough. Pain, nausea, vomiting, dehydration, weakness, and loss of weight are all common to many lesions of the upper part of the abdomen. The finding of occult bleeding in the stool merely intensifies the search for its source. Some authors have commented on the presence of fever with the peripapillary growths, which they claim is not present with other duodenal lesions. Odelberg, as well as others, emphasized the presence of bile in the vomitus as an important differentiating diagnostic feature in considering the possibility of an infrapapillary tumor. The physical findings reported in the literature are not of much diagnostic help. Most authors agree that the lesion is in an extremely late stage when a mass is palpable, and that upper abdominal tenderness may indicate the same hopeless situation.

The diagnosis of an infrapapillary duodenal malignant tumor is usually a roentgenologic one. Weber and Kirklin,[18] reporting on malignant tumors of the entire small intestine studied at the Mayo Clinic between 1930 and 1939, noted that a correct roentgenologic diagnosis of a lesion localized in the small intestine was made in 31 of 36 cases. In 17 of these cases, the tumors were duodenal, and 7 of these were in the infrapapillary portion. A tumor was identified in all 7 instances, being specifically labeled as "tumor" in 6 cases and as "an obstructive lesion" in the other. Dixon's group believed that the roentgenologist may offer a diagnosis of a "lesion," a "filling defect," a "polyp," or a "constrictive defect," and that, although these are not ideally precise terms, they give the connotation of neoplasm and lead the surgeon to the correct approach. These authors considered that a roentgenologic diagnosis hardly could be expected to be more precise than a gross pathologic one.

With regard to the treatment of these malignant lesions, Hoffman and Pack,[10] along with Dunhill,[7] and Jordan and De Bakey,[13] suggested that wide segmental re-

section of the duodenum and jejunum, with end-to-end anastomosis, should be the ideal therapy whenever possible. Many of the tumors reported in the literature have arisen near the duodenojejunal junction, and these appear to be technically amenable to segmental resection if they are discovered early enough. Metastatic lesions from these tumors are rather late in onset, and thus surgical resection might be expected to be successful. When tumors are located in this distal part of the duodenum, they are said not to involve the pancreas, and many surgeons have commented that resection does not require partial pancreatectomy if the lesions are found early in their course. Other surgeons, however, believe that a much more radical operation is necessary and that pancreatoduodenectomy is to be seriously considered. Because of the lymph drainage of the duodenum, Weinberg[19] stated that, no matter which portion of the duodenum is involved, a Whipple type of pancreatoduodenectomy with thorough removal of the regional lymph nodes should be performed if the operation is to be considered at all curative in nature.

The surgical mortality rate reported in many of the articles has ranged between 20 and 30 per cent. Review of the literature is complicated in this regard, since tumors in certain parts of the duodenum are treated by a much more extensive procedure than are those in other portions. In addition, so few patients are treated by a single surgeon or group of surgeons that significant mortality rates are not to be found.

With regard to 5-year survival rates and other survival studies, the scarcity of cases again renders quotations from the literature rather futile. We noted reports of several instances in which surprisingly long survival without recurring disease was attained. In sarcoma of the duodenum, the lesions apparently are considerably smaller, with metastasis being later and the prognosis accordingly better. Since certain of these lesions contain lymphosarcomatous elements that are reported to be radiosensitive, many authors have commented that a course of radiation therapy should be given over the general region of the duodenum and its environs early in the postoperative period. We found no series significantly large enough for a presentation of comparative results, however.

PRESENT STUDY

The surgical pathologic files of the Mayo Clinic for the years 1915 through 1954 were reviewed to obtain the material for study of all cases of infrapapillary duodenal tumor in which surgical treatment was used. Only those cases were included in which operation had been performed at the clinic and in which tissue was available for pathologic survey. Thus, it was possible to determine the outcome in patients who had undergone definitive resection, as well as to follow the course of those who had undergone palliative procedures. From these records, the pertinent clinical data, including the history, physical findings, laboratory reports, and x-ray examinations, were abstracted. The surgical operations were reviewed and the findings were noted. Pathologic studies were made on every specimen. The gross lesions were available in the cases in which surgical resection had been performed. New sections were cut from the lesions, from the regional lymph nodes, and from any surrounding tissue that appeared suspicious. In those cases in which only biopsy had been possible, the microscopic specimens were reviewed, with new preparations frequently being made from the original biopsy material. As a result, 30 surgical cases of primary infrapapillary duodenal tumors were accepted as suitable for this series, representing a 40-year period.

Benign tumors.

Clinical features. Six of the 30 tumors were benign. The oldest patient with a benign lesion was 78 years of age and the youngest was 26, the average being 51. There were 3 men and 3 women. The lack of symptoms was significant, since 4 of these patients had been operated on for other reasons and the duodenal tumors were incidental findings. Two of the patients had

duodenal ulcers confirmed roentgenologically that led to the surgical intervention. Two others had cholelithiasis and were undergoing cholecystectomy at the time of discovery. The fifth patient had a large leiomyoma with central ulceration that had produced a 5-month history of rather severe melena, with considerable epigastric pain after meals. The sixth patient had an adenoma associated with a 5-year history of distress after meals. A bout of hematemesis had occurred on one occasion 6 months prior to operation.

Obviously, 4 of these 6 patients had not experienced any physical manifestations referable to their tumors. Epigastric tenderness was recorded in the fifth patient and was suggested in the other. Laboratory data were within normal limits save for those on the one patient with a myoma of the duodenum, who had only 7 Gm. of hemoglobin per 100 ml. of blood. This patient also had a bleeding duodenal ulcer, so the laboratory findings were not specific. The patient with the huge leiomyoma with ulceration and repeated melena had been given numerous blood transfusions before admission, so that current values for hemoglobin were not diagnostic.

Roentgenologic examination of the stomach and duodenum was carried out in 5 of these 6 patients. A positive diagnosis was made in only 1 case, that of the leiomyoma. In the remaining 4, the diagnosis was duodenal ulcer in 2 cases and a "negative" duodenum in 2. It is to be remembered that specific study of the terminal part of the duodenum was not the object of some of these examinations. The stomach was being examined, and the first portion of the duodenum was outlined clearly. Whether more specific roentgenologic studies of the upper part of the small intestine would have yielded a higher percentage of positive findings is a matter of conjecture.

Surgical considerations. In 4 of these 6 patients with benign infrapapillary duodenal tumors, definitive surgical treatment was being undertaken for other indications. Removal of the duodenal tumor was a purely incidental surgical procedure and presented no difficulty. In the other 2 patients, laparotomy was undertaken primarily for the duodenal tumor. In each of these cases, excision was sufficient and radical resection was not required. All patients survived and gave no evidence of recurrence during the follow-up period.

Pathologic features. Our review of the specimens corroborated the original diagnoses, which included 4 leiomyomas, 1 accessory pancreatic nodule, and 1 adenoma. The largest tumor of this group was a leiomyoma that measured 7 by 5 by 5 cm. The pancreatic rest was 2 cm. in diameter and was located along the inferior border of the descending portion of the duodenum just distal to the papilla. The adenoma was 5 mm. in diameter and also was located on the inferior border of the duodenum.

Malignant tumors.

Clinical features. The youngest patient in this category was 38 years of age, and the oldest was 73. Both were men. The average age for the entire group was 57 years. The group included 12 men and 12 women.

The subjective symptoms were those commonly associated with many upper abdominal syndromes and there was nothing particularly distinguishing about them. Only 1 of the 24 patients had an acute onset of symptoms, which took the form of nausea and vomiting. The onset in all other instances was much more gradual. The average duration of symptoms was 14 months, the longest history being 6 years and the shortest 4 weeks. The average duration of symptoms in patients who had surgically resectable lesions was 20 months, while it was only 9 months in patients with nonresectable growths. Pain was the outstanding symptom in this group, occurring in 17 of the 24 cases. It was usually described as being of the nature of a colic, but occasionally it was a dull, persistent ache. In a few cases, such terms as "soreness," "tenderness," or "burning" were common in the history. The pain was located in the epigastrium in 13 cases and in various areas in the others. Extension of pain to the back or the costal

margins was described in 7 instances. In 7 patients, the pain appeared 30 minutes to 5 hours after meals, and 5 patients stated that relief could be produced by vomiting. Bloating, belching, sour eructation and fullness after eating were noted frequently but apparently were not specific. Anorexia was noteworthy in 15 persons. Vomiting was frequent in 15 of the 24 patients. Four patients reported the presence of bile in the vomitus, but specific descriptions of the vomitus were lacking in many instances. The vomitus was definitely bloody in 2 patients. A change in bowel habit was reported by 12 of the 24 patients. Eleven of these noted definite constipation, while diarrhea alternated with constipation in the other. Definite loss of weight occurred in 18 patients, varying from 80 pounds in one to as little as 5 pounds in another, the average being 21 pounds over a 9-month period.

Six patients complained chiefly of anemia. The anemia in 5 of these had been reported prior to admission to the clinic. The value for hemoglobin was less than 8 Gm. in all 6 patients. Two of these 6 patients also reported melena. Of the 24 patients with malignant tumors, 6 had proved melena, and all but 1 of these 6 showed hemoglobin readings of less than 10 Gm. Hematemesis was reported in only 2 instances. Both these patients had large ulcerating lesions, one polypoid and one stenosing.

None of the patients in the entire series had ever been jaundiced.

The 24 patients could be divided into 3 groups according to their symptoms. In the first group (14 patients) were those who had symptoms of obstruction. In the second group (8 patients), bleeding was the outstanding characteristic, with melena or hematemesis leading to the discovery of anemia and obviously being the source of the weakness and fatigue of which the patients complained. The third group was composed of 2 patients who had pain as the chief complaint.

Examination at the clinic revealed that 9 of the patients exhibited enough pallor to be commented on at the time of the initial visit. Only 6 patients had definite tenderness in the epigastrium or elsewhere in the abdomen. An abdominal mass was noted in 6 patients, and 4 of them had lost an average of 25 pounds. Only 2 of these patients with palpable masses had resectable tumors. Hepatomegaly was reported in 3 patients, and only 1 had a resectable tumor. Results of physical examination were entirely normal in 5 of the 24 patients.

The laboratory findings were somewhat more significant than were the history and physical examination. The value for hemoglobin in 13 patients was less than 11 Gm., and 10 of the 13 had less than 9 Gm. The lowest hemoglobin reading (5.3 Gm.) was in a patient who had a large sessile ulcerating adenocarcinoma. Special blood smears for morphologic diagnosis were examined from all patients with anemia. In every case, hypochromasia was reported, associated usually with microcytosis and polychromasia. Stool examinations were carried out in 5 of the 13 anemic patients and were positive for occult blood on at least 1 occasion in all 5. The sedimentation rate of the erythrocytes was recorded in 12 of the 24 cases. In 10 of these, the rate was greater than 20 mm. during the first hour (Westergren method). The average rate for this group was 48 mm., the highest being 121 mm. Analysis of gastric contents after an Ewald test meal was reported in 17 of the 24 patients. Seven of these were completely achlorhydric, while 3 showed low readings for free hydrochloric acid. Six had normal values for free acid. In 1 patient, who had liposarcoma, the value for free acid was 60 U. The achlorhydria or hypochlorhydria appeared to be related to obstruction of the terminal part of the duo-

Table I. *Accuracy of roentgenologic diagnosis in malignant infrapapillary duodenal tumors*

Roentgenologic findings	*No. of cases*
Correct diagnosis	9
Correct localization, with description of lesion	6
Probable malignant tumor	4
Probable benign tumor	2
Suspicion of a lesion	2
Total	23

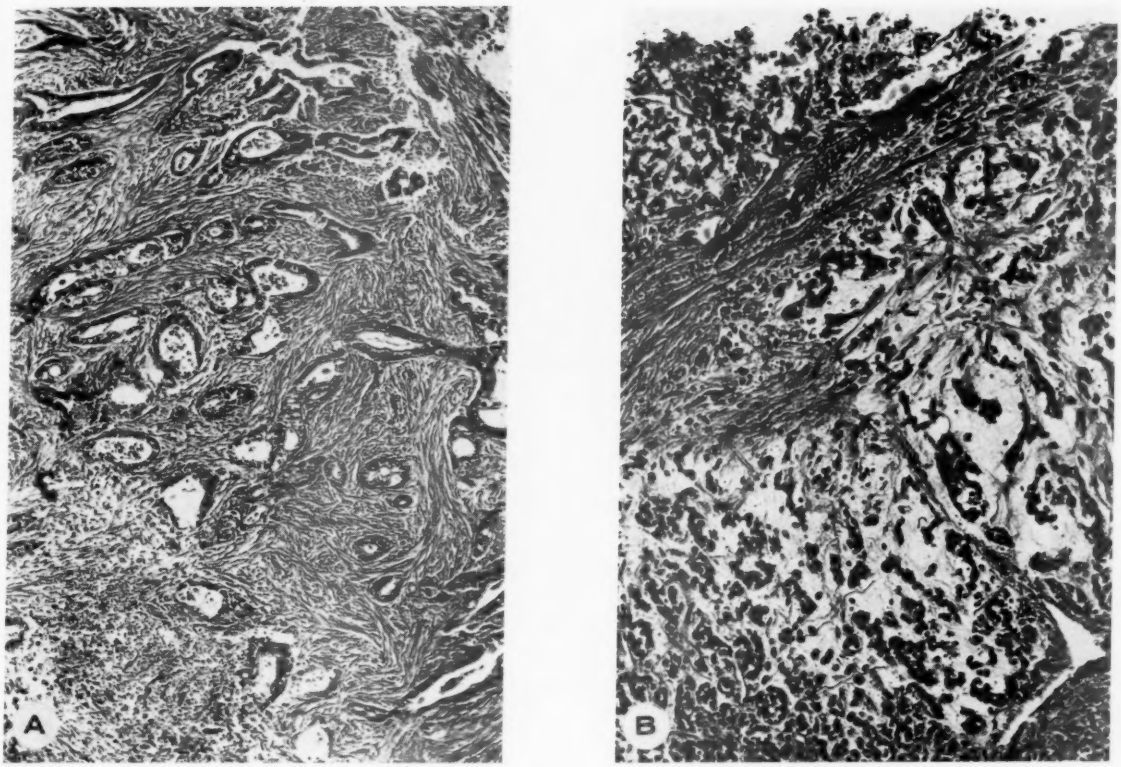

Fig. 1. *A,* Grade 1 adenocarcinoma of duodenum. (Hematoxylin and eosin; ×60.) *B,* Grade 4 adenocarcinoma of duodenum. (Hematoxylin and eosin; ×85.)

denum, since gastric retention was a significant feature in these cases and the subsequent neutralization of the free acid was probably the responsible factor.

Roentgenologic examination of the stomach and duodenum proved to be most helpful in establishing the diagnosis. It was carried out in 23 of the 24 cases of malignant tumors (Table I). Certain lesions were described as being annular, polypoid, ulcerating, or constricting in the absence of an absolute roentgenologic diagnosis. Such descriptions helped the clinician to arrive at the proper course to be followed. The roentgenologist either described or at least recognized within the infrapapillary part of the duodenum 21 of the 23 tumors submitted to roentgenologic study. In 12 instances, this diagnosis was possible at the original examination of the stomach and duodenum. In 7 patients, 2 attempts were necessary. In 3 patients, additional roentgenologic studies of the small intestine were carried out to delineate further the nature of the lesion. In the remaining patient, "duodenal ulcer" was the primary diagnosis but a second roentgenologic examination of the stomach and duodenum performed 7 weeks later because of progression of symptoms revealed the infrapapillary duodenal carcinoma. Thus, in only 2 instances was the diagnosis either incorrect or misleading. In 2 other patients, the lesion was not seen. However, both these patients had other intra-abdominal pathologic lesions demonstrated roentgenologically that led to surgical intervention.

Pathologic features. The great majority of the malignant tumors were adenocarcinomas (Fig. 1). The classification of all the malignant tumors is presented in Table II. Carcinoids were not encountered in this series. The treatment in 1 of the 12 cases in which complete resection of the tumor and surrounding tissue was possible actually was listed as palliative, since there was evidence of metastasis to a left supraclavicular lymph node. The specimens obtained at resection were divided into 2 main groups on the

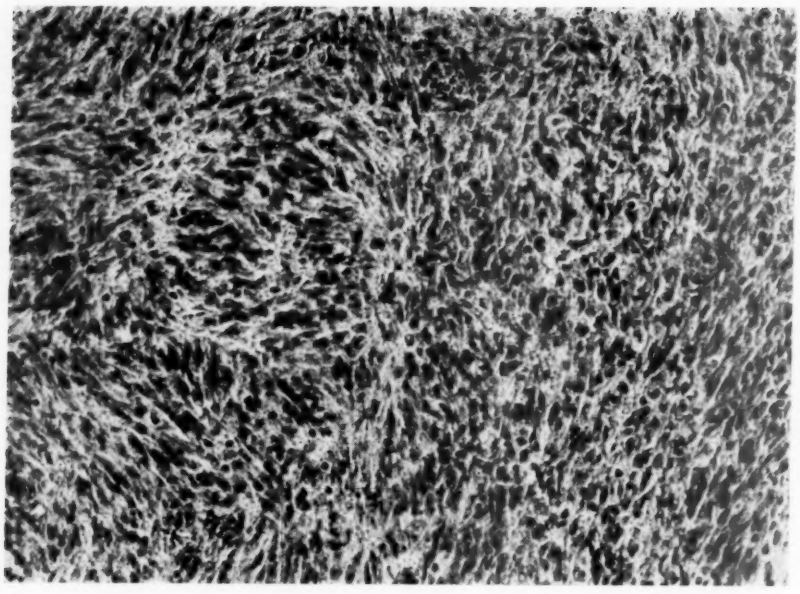

Fig. 2. Leiomyosarcoma of duodenum. (Hematoxylin and eosin; ×190.)

basis of gross appearance, the first category being annular constricting lesions and the second being polypoid tumors of the sessile variety. Almost all of the tumors showed some ulceration. The annular stenosing lesions showed more tendency toward infiltration of the duodenal wall than did the polypoid type. There were 4 polypoid growths and 1 extremely broad, flat, sessile tumor. The 1 leiomyosarcoma was a smooth polypoid lesion with typical central ulceration (Fig. 2). The largest resected lesion was an adenocarcinoma measuring 10 by 6 by 2 cm. The smallest was an annular stenosing adenocarcinoma measuring 3 by 2 by 1 cm.

In 8 of the 12 resected specimens, including the leiomyosarcoma, the lymph nodes were free of metastatic lesions. Seven of these 12 specimens revealed malignant invasion of the perineural spaces, and 5 tumors had associated inflammatory changes extending to the formation of small abscesses. In 7 lesions, the malignant process had not extended through the wall of the duodenum and there was no evidence of peritoneal involvement. In the remaining 5 specimens, pronounced peritoneal extension was obvious. The leiomyosarcoma was well localized and had not invaded the peritoneum.

In the 2 patients in whom radical pancreatoduodenectomy had been performed, extension of the tumor was found. In one of these, the extension was directly into the pancreas, whereas in the other, the pancreatic lymph nodes were involved but the parenchyma was not. There were 1 adenoacanthoma and 1 liposarcoma (Fig. 3).

Surgical considerations. Of the 24 patients who underwent surgical treatment for malignant tumors, 12 were judged to have nonresectable lesions either because distant metastatic deposits were identified or extensive local invasion with complete fixation was found. Table III shows the area of involvement or the reason for the decision concerning nonresectability. In these 12 cases, 10

Table II. *Classification of 24 malignant infrapapillary duodenal tumors*

Type of tumor	*Grade of malignancy*				*Total*
	1	*2*	*3*	*4*	
Adenocarcinoma	2	10	5	4	21
Adenoacanthoma	0	0	0	1	1
Leiomyosarcoma	1	0	0	0	1
Liposarcoma	1	0	0	0	1
Totals	4	10	5	5	24

palliative bypassing procedures were performed to relieve the obstruction. In the other 2, obstruction was not a feature and biopsy was the only surgical procedure. The bypassing procedures included 7 gastroenterostomies and 3 duodenojejunojejunostomies.

Eleven of the 12 patients with nonresectable lesions were dead within 2 years. One patient died in the hospital in the immediate postoperative period, and 5 were dead within 6 months of their dismissal from the clinic. One patient lived 9 months, one 10 months, one 12 months, and two 24 months postoperatively. The fate of the twelfth patient is unknown.

Of the 12 patients whose lesions were resected, 2 underwent radical pancreatoduodenectomy of the Whipple type and the other 10 had segmental resection with end-to-end anastomosis. Five of the 12 died in the immediate postoperative period. Four of them had undergone segmental resection and the fifth had been subjected to radical pancreatoduodenectomy.

Of the 7 patients who survived resection, 4 were living and well without evidence of recurrence 19, 16, 12, and 5 years, respectively, after operation. All of these had undergone segmental resection. One was the patient with the leiomyosarcoma, whereas the other 3 had adenocarcinomas, 2 of them grade 2 and one grade 3 on the Broders scale. All had localized lesions, with no involvement of lymph nodes and no evidence of peritoneal extension. Of the remaining 3 patients, 1 died of recurrent carcinoma 51 months after operation. The second patient recently had experienced recurrence of the lesion 26 months after operation and metastatic lesions were detected in the vaginal vault. She was still living at last report after receiving a course of palliative roentgen therapy. The third patient underwent palliative resection and was hospitalized 4 months afterward elsewhere with evidence of recurrence.

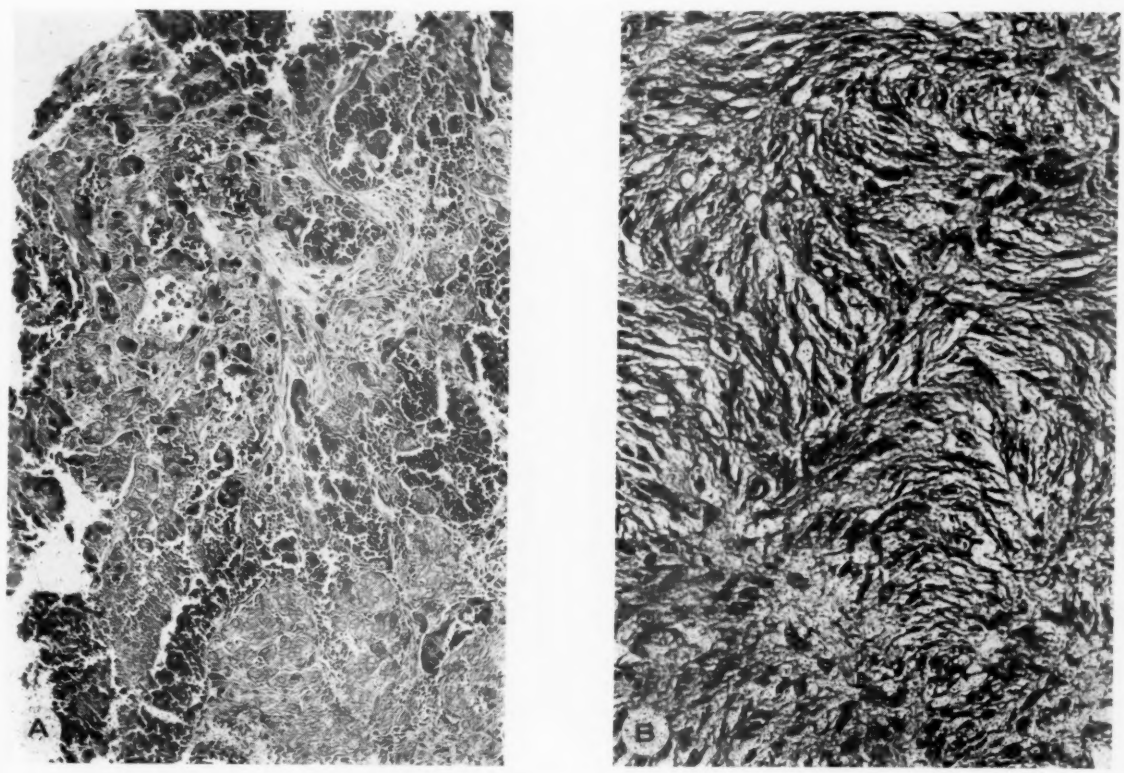

Fig. 3. *A,* Metastatic tumor in lymph node from adenoacanthoma of duodenum. (Hematoxylin and eosin; ×65.) *B,* Liposarcoma of duodenum. (Hematoxylin and eosin; ×180.)

Table III. *Spread of neoplasm in 12 nonresectable malignant infrapapillary duodenal tumors*

Site of spread	*No. of cases**
Lymph nodes	9
Mesenteric	5
Aortic	2
Celiac	1
Retroperitoneal	1
Liver	3
Complete local fixation	3
Transverse mesocolon	1
Lesser omentum	1
Greater omentum	1
Peritoneal implants	1

*More than one site of spread in several cases.

She presumably has died of the disease.

Thus, 12 of the 24 malignant tumors were considered nonresectable and nothing was done aside from simple biopsy or a palliative operation to relieve obstruction. The remaining 12 patients underwent resective procedures, eleven of the operations were performed with some hope of cure but one was considered palliative because of supraclavicular metastasis. Four of the 11 patients were living 5 to 19 years postoperatively. Three of the remaining 7 patients had evidence of recurrence of the lesion some 4 months to 4 years after operation. Two died, and 1 was living 30 months after resection but had metastatic spread in the pelvis. The lesions in these 7 patients were adenocarcinomas with evidence of serosal involvement, and 1 of them had extended to the lymph nodes and the pancreas as well. Five patients did not survive operation.

DISCUSSION

Four of the 6 benign tumors in this series of 30 infrapapillary lesions of the duodenum were myomas. Benign tumors in this location usually are found incidentally. Only 2 of the growths produced any symptoms. All were easily removed surgically by local excision and presented no further problem.

With regard to malignant tumors, our series differed from those previously reported in that 21 per cent of the patients were less than 50 years of age, but the incidence by pathologic classification was similar to that of other reports. Only 1 of the malignant tumors was of the mucus-producing variety. In accord with previous reports, our patients presented symptoms primarily associated with obstruction or bleeding. The majority of the lesions were of an obstructive nature and the surgical findings correlated well with the symptoms. Annular stenotic tumors usually were found, but several polypoid lesions were obturative and also obstructive. One-third of the patients had symptoms related to bleeding and its sequelae. Study of the surgical specimens revealed that, regardless of the other gross characteristics, all presented sufficient ulceration to account for rather severe loss of blood. When bleeding was the primary complaint, 75 per cent of the lesions were resectable, whereas only 26 per cent were resectable when obstruction was the chief difficulty. It would appear that growths in this portion of the duodenum that ulcerate and bleed are much more likely to be detected early before they have exceeded the limits of resectability. The symptom complex of pain alone was relatively minor and accounted for only 2 cases. By the time the diagnosis was sufficiently evident to lead to surgical intervention, pain usually was associated with numerous other symptoms.

The presence or absence of bile in the vomitus was not important in attempts to distinguish the infrapapillary lesions from those located more proximally in the duodenum. Of the 15 patients with vomiting, only 4 described bile in the vomitus.

The average duration of symptoms for the patients with malignant tumors was 14 months. We thought it odd that the duration of symptoms in the patients who underwent resection was 11 months longer than it was in the group who had nonresectable lesions. The lesions in the latter group apparently were not of the character to produce bleeding.

Physical findings were not of much diagnostic help. By the time a palpable mass was detected, surgical intervention was of little avail. Pallor was helpful, but it is such a nonspecific finding that numerous other

diagnostic aids are required. In 20 per cent of our patients, results of physical examination were entirely normal.

Laboratory data were not of great significance except for a high incidence of anemia. As already noted, the relatively great incidence of achlorhydria or hypochlorhydria was explained on the basis of gastric retention secondary to obstruction in the distal part of the duodenum, with retention of the highly alkaline duodenal contents within the stomach.

Our study bears out well the assertion that the diagnosis of malignant infrapapillary duodenal neoplasms may well be a radiologic one. In almost every case, not only was a tumor detected roentgenologically but significant comments concerning it were also made and led to the proper course of therapy. Actually, in only 2 of our patients was operation undertaken without prior knowledge that a specific pathologic lesion was present in this particular zone. However, a single roentgenologic examination may be insufficient to identify the lesion.

It has been suggested that malignant lesions of this type may be treated as adequately by segmental resection as by radical pancreatoduodenectomy of the Whipple variety. Some authors have thought that comparable survival rates are the rule and that greatly reduced morbidity and mortality rates will be noted after the less radical procedure. In our 12 cases in which resection was performed, the pancreas appeared to be grossly involved in only 2. After pancreatoduodenectomy, this was proved in only 1 instance. In 8 of the resected specimens, none of the regional lymph nodes were involved, and penetration of the duodenal wall or serosa could not be demonstrated in 7. This suggests that segmental resection may well be preferable in cases in which the diagnosis is made early.

Of the 12 patients who underwent resection, 10 were treated by segmental resection and 2 by the radical Whipple procedure. Four of the 12 were living and well 5 to 19 years postoperatively, and all of them had undergone segmental resection. Pathologic studies confirmed the impression that they all had favorable lesions, since neither the lymph nodes nor serosa was involved. Unfortunately, 5 of the 12 patients who underwent resection died in the immediate postoperative period, which is a somewhat higher mortality rate than the 25 to 30 per cent usually reported in the literature. The other 3 patients who survived operation all died of their original disease.

SUMMARY AND CONCLUSIONS

A study was made at the Mayo Clinic of 30 cases in which tumors of the infrapapillary portion of the duodenum were encountered surgically. Twenty-four of the tumors were malignant and 6 were benign.

Four of the benign neoplasms were incidental findings, whereas bleeding was the cardinal symptom in the other 2. All were readily removed, with eminently satisfactory results.

Of the patients with malignant lesions, 21 per cent were under 50 years of age. The average duration of symptoms was 14 months. In 59 per cent of these patients, the chief problem was obstruction, and only 36 per cent of this group presented resectable lesions. Bleeding was the prime factor in 33 per cent of the 24 patients with malignant lesions, yet 75 per cent of the tumors in this group were still resectable. In only 8 per cent of the patients was pain the chief symptom.

Pallor or a palpable mass or both made up the only significant physical findings in the group with the malignant tumors. In 20 per cent of the patients, the results of physical examination were essentially normal. No patient was jaundiced at any time.

Roentgenologic studies were extremely helpful in the diagnosis of the malignant neoplasms. A lesion in the infrapapillary part of the duodenum was reported in 91 per cent of the patients.

Only half of the malignant tumors were resectable. Segmental resection was performed in 10 cases and radical pancreatoduodenectomy in 2. Eight of the specimens showed no metastatic involvement of the lymph nodes. Malignant invasion of the

pancreas was proved in only 1 of the specimens from the patients in whom pancreatoduodenectomy was carried out.

One-third of the patients who had resection were alive and well 5 to 19 years after operation for the malignant tumors. All of them had undergone segmental resection.

Twelve (50 per cent) of the malignant lesions were beyond surgical resection. In 10 of the patients, palliative bypassing procedures were performed to relieve obstruction. One of the patients died in the immediate postoperative period and 10 others were dead within 2 years. The fate of the twelfth patient is unknown.

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The influence of fluid therapy upon water and electrolyte equilibria and upon the circulation during the shock period in burned patients

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Modern understanding of the physiologic changes which occur during experimental burn shock began with the observation by Underhill[31] that the composition of burn blister fluid was essentially the same as that of plasma. Later Blalock[4] demonstrated that the hypotension of dogs after thermal trauma could be accounted for by the local loss of fluid into the injured areas. The work of Rosenthal,[27] Tabor,[30] Millican,[20] and Fox[9] in burned mice showed the capacity of the injured area to swell and to absorb administered fluids, electrolytes, and proteins with the subsequent decrease in blood volume and dehydration of the uninjured tissues. A recent review by Rosenthal and Millican[26] summarizes the cumulated knowledge obtained from animal experimentation.

A galaxy of investigators have described physiologic changes associated with thermal trauma in man. These changes include the augmented activity of the adrenal cortex,[7, 14, 18, 34] disturbances of water and electrolyte equilibria,[5, 8, 21] and alterations of the circulation[12, 15, 23, 25] but in general these data were collected on a small number of patients, often after the shock period has passed, with little attention paid to the consequences of varying the therapy.

The purpose of the present study was twofold, first, to determine whether the composition of the fluid therapy administered during the shock period can influence the response of the circulation and fluid balance and, second, to determine whether laboratory measurements can elucidate the physiologic mechanisms involved in the success or failure of the therapy administered as judged on the basis of survival of the patients treated.

The Peru Project now in progress in Lima, Peru, afforded an excellent opportunity to study these problems, since a well-controlled evaluation of the effect of therapy upon mortality rate during the shock period was being made on a large number of burned patients.[16, 17] In that study the fluid used for therapy in one group of patients contained large amounts of sodium (saline solution alone or combined with plasma), while the fluid used in another group contained only small amounts of sodium (plasma supplemented with glucose and water). Patients were strictly alternated between these therapy groups.

The results of these studies in adults have clearly shown that saline solutions alone are indeed effective as therapy during the shock period. In 79 burned adults treated with large amounts of sodium, no deaths

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Supported by a grant from the National Institutes of Health, Bethesda, Md.

Received for publication June 13, 1960.

occurred during the shock period, whereas 12 per cent of the 74 adults treated with small amounts of sodium died during the shock period. The results in children demonstrate that saline solutions alone were as effective as treatment with plasma supplemented by glucose and water, since the mortality rate during the shock period in a total of 110 burned children was 20 per cent in both groups. When plasma was added to saline solution, the mortality rate significantly decreased in burned infants and children. In this latter therapy comparison, the mortality rate during the shock period was 19 per cent in the saline-treated group and 9 per cent in the group treated with saline and plasma.

This publication will report various laboratory measurements of the circulation and fluid balance taken during the first 48 hours after injury in a series of 153 burned adults and 184 burned children from Peru. In order to avoid confusion, the data on the adult therapy comparison will be presented separately from data on the therapy comparisons in children.

MATERIALS AND METHODS—ADULTS

One hundred fifty-three adults between the ages of 12 to 73 years were studied. Ninety per cent of the patients suffered burns from flames, while the rest were from hot fluids. If the burn involved 10 per cent or more of the body surface area, the patient was placed into one of two therapy groups, "saline" or "colloid," with strict alternation of therapy practiced between these groups. The patients in the saline group received an average quantity of an isotonic saline solution by oral and/or intravenous routes equivalent to 10 per cent of body weight during the first day after thermal trauma and half that amount the second day. The saline solution administered orally contained 140 mEq. per liter of sodium, 93 mEq. per liter of chloride, and 47 mEq. per liter of bicarbonate, while the solution given intravenously contained 141 mEq. per liter of sodium, 114 mEq. per liter of chloride, 28 mEq. per liter of lactate, and 1.5 mEq. per liter of calcium. No additional liquid or food was administered either orally or intravenously. Blood, plasma, or colloid was not given to these patients during this 48-hour period.

The patients in the colloid group received during the first 48-hour period after thermal injury a quantity of plasma, blood, or polyvinylpyrrolidone (84 per cent of the patients received only plasma as their colloid therapy) equivalent to 2.7 per cent of body weight supplemented by a quantity of glucose and water equivalent to 7.3 per cent of body weight. The colloid was administered by the intravenous route while the water was given by mouth and the glucose and water was administered intravenously. The quantity of colloid given was 40 per cent of that recommended by Evans,[8] but represents more than the amount previously available for burned patients in Peru.

All accessory therapy was identical in the groups compared simultaneously and consisted chiefly of measures routinely employed in the hospitals. The exposure method of local treatment of the burned area was used throughout.

Blood determinations. Ten milliliters of blood was withdrawn from the femoral, jugular, or anticubital veins into a heparinized syringe on the patient's admission to the hospital and at intervals of approximately 8, 18, 24, and 48 hours after burning. Within 1 hour after collection of the blood determinations were made of hematocrit by centrifugation of the blood at 3,000 r.p.m. for 30 minutes, plasma sodium and potassium by analysis in the flame photometer with lithium as internal standard,[2] plasma chloride by the method of Van Slyke and Hiller,[32] plasma alkaline reserve by the manometric method of Peters and Van Slyke,[24] and total plasma protein by the method of Van Slyke and associates.[33]

Plasma volume. Plasma volume was measured in 33 adult patients by the 4-sample technique of Noble and Gregerson[22] with T-1824 on admission to the hospital or within the first 12 hours after burning and

later at the end of 24 and 48 hours after burning. When hemolysis or lipemia were present macroscopically in the plasma without dye, the cellulose technique of Allen[1] was used to eliminate the error due to these factors.

Renal function. Glomerular filtration and renal plasma flow were determined in 17 adult patients, 13 of whom were in the saline group, at the termination of 24 or 48 hours after burning. The technique of Goldring and Chasis[11] was used with inulin[28] and sodium para-aminohippurate.[29] From the urine samples collected during the three 20 to 45 minute clearance periods, the total excretion of sodium and potassium in milliequivalents per minute was calculated. In addition, 19 adult saline-treated patients who had received their saline solution exclusively by the oral route were catheterized on admission to the hospital and urine samples were collected at 2-hour intervals. The volume of each sample was measured and the urine analyzed for sodium and potassium concentration.

Water and electrolyte balance. Water and electrolyte balance was studied in 54 adult patients who did not vomit or present diarrhea during the shock period. Fluid intake and urinary output were carefully measured over each 24-hour period, and at the end of each period the net water balance was determined by accurately weighing the patient in a stretcher balance. To estimate all of the water losses, an approximate value of 800 ml. was used for insensible loss each day, and the local loss from the burned area into the bed sheets was calculated from the formula: local fluid loss in ml. = [fluid intake in ml. – (urine in ml. + insensible loss in ml.)] – [change of weight in grams (Gm. $\simeq$ ml.)]. The intake of sodium and potassium was determined in the fluids administered during each 24-hour period by analyses in the flame photometer, while the output of these ions was measured only in the 24-hour urine collections. To calculate the total loss of both ions the insensible loss was disregarded and the local loss was calculated by:

0.95* × plasma Na^+ or K^+ in mEq. per liter × liters of calculated local fluid loss

electrolyte balance = cation intake – (urine cation loss + calculated cation loss locally).

Statistical analysis. The probability of 0.05 ($p = 0.05$) was chosen as the level for statistical significance. A difference is judged as statistically significant only when the calculated t equals or exceeds the tabulated t at a probability of 0.05 with the pertinent degrees of freedom.

RESULTS IN ADULTS

Fluid and electrolyte balance. Table I lists the data obtained and calculated from a study of 54 burned adults who had no vomiting or diarrhea during the first 48 hours after thermal trauma. Only in patients with burns of 10 to 50 per cent body surface area were the numbers sufficiently large to analyze statistically. The fluid loss from the burned area was calculated with an assumed value of 800 ml. for the insensible loss. This assumption was necessary for a more accurate estimation of sodium balance, since the loss of sodium into the bedclothes might be more than the loss by the kidneys.[21]

Water balance. In general, patients with burns involving 10 to 50 per cent of the body surface area treated with saline solutions showed a positive balance on each day during the first 48-hour postburn period, while those treated with colloid and water showed a negative balance on each day. In the saline-treated patients, the positive balance was marked on the first day after burning but only slightly positive on the second day, and the difference in fluid retention as measured by body weight gain on the first postburn day was not significantly greater in the patients with 26 to 50 per cent burns than in patients with 10 to 25 per cent burns.

Because the saline group received approximately 1½ times more fluid than the

*The concentration of Na^+ and K^+ in the extracellular fluid is 0.95 times the concentration in the plasma.

Table I. *Water and ion balance in burned adults*

Balance	% burn	Therapy group	First day: No. of cases	First day: Intake	First day: Urine	First day: Urine (% excreted)	First day: Insensible	First day: Local loss	First day: Balance*	Second day: No. of cases	Second day: Intake	Second day: Urine	Second day: Urine (% excreted)	Second day: Insensible	Second day: Local loss	Second day: Balance
Water				(ml.)	(ml.)	(% excreted)	(ml.)	(ml.)	(ml.)		(ml.)	(ml.)	(% excreted)	(ml.)	(ml.)	(ml.)
	10-25	S	18	5,547	998	18.0	800	1,705	+2,044	16	2,826	1,198	42.4	668†	583	+377
		C	11	2,744	959	34.9	800	1,003	− 18	9	2,524	1,435	56.9	782†	1,018	−711
	26-50	S	14	5,492	646	11.8	747†	1,915	+2,184	13	2,936	799	27.2	765†	1,356	+ 16
		C	5	2,364	432	18.3	800	1,431	− 300	3	2,203	734	33.3	800	902	−233
	51-100	S	2	5,175	491	—	800	1,489	+2,150	2	2,650	734	—	800	1,466	−350
		C	4	3,095	238	—	800	1,582	+ 475	3	3,390	348	—	800	1,842	+400
Sodium				(mEq.)	(mEq.)			(mEq.)	(mEq.)		(mEq.)	(mEq.)			(mEq.)	(mEq.)
	10-25	S	18	760	164	—	—	246	+ 350	16	387	228	—	—	79	+ 80
		C	11	46	56	—	—	116	− 126	9	29	21	—	—	133	−125
	26-50	S	14	753	88	—	—	254	+ 411	13	404	111	—	—	178	+115
		C	5	61	41	—	—	189	− 169	3	37	7	—	—	123	− 93
	51-100	S	2	716	51	—	—	194	+ 471	2	370	18	—	—	191	+161
		C	4	179	17	—	—	212	− 50	3	115	8	—	—	249	−142
Potassium																
	10-25	S	18	0	69	—	—	7	− 76	16	0	55	—	—	3	− 57
		C	11	2	38	—	—	4	− 40	8	1	45	—	—	4	− 48
	26-50	S	14	0	99	—	—	8	− 107	13	0	73	—	—	6	− 79
		C	5	3	36	—	—	6	− 39	3	2	58	—	—	4	− 60
	51-100	S	2	0	43	—	—	7	− 50	2	0	52	—	—	6	− 58
		C	4	7	36	—	—	7	− 36	3	5	25	—	—	8	− 28

*Balance was determined by accurately weighing the patient in a stretcher balance. The insensible loss of electrolytes was disregarded in the calculation of ionic balance.

†An average value below 800 ml. denotes that one or more patients in the group had to be assigned values less than the assumed value in order to avoid negative values for local fluid loss.

colloid group during the 48-hour postburn period, urine values have to be compared as the per cent of fluid excreted via the kidney for fair appraisal of any difference between the groups. Although the differences were not statistically significant, the colloid group showed a higher average percentage of fluid excreted by the kidneys on both days in patients with less than 50 per cent of the body surface area burned. The saline-treated patients, however, showed a significantly lower percentage of fluid excreted via the kidneys in the patients with 26 to 50 per cent burns on both postburn days compared with the patients with 10 to 25 per cent burns. In the saline group, when the fluid intake was equal in the patients with 10 to 25 per cent and the patients with 26 to 50 per cent burns, the total 48-hour extrarenal losses (total 48-hour insensible loss plus total 48-hour calculated fluid loss into the bed sheets) were significantly greater in patients with the more severe burns. This finding would be expected, since the urine volume decreased significantly while the body weight increased only slightly as the extent of the burned area increased.

Sodium balance. In general, the balance was markedly positive for the saline group on a high sodium intake while the balance was negative for the colloid group on a low sodium intake. The balance became more positive as the extension of the burned area increased in the saline-treated patients. In the colloid group, there was no notable correlation of negative balance with the more severe burns.

Comparison of the urinary sodium excretion of the two therapy groups showed that the saline group had significantly higher values than the colloid group on both days in the patients with 10 to 25 per cent burns and on the second day in the patients with 26 to 50 per cent burns. In both groups considered individually there was a significantly decreased excretion of sodium in patients with the more severe burns on the second day.

Potassium balance. As could be expected, both saline and colloid groups showed a negative potassium balance in all burns studied, since intake of potassium was almost nil. The saline group demonstrated a significantly higher urinary potassium excretion than the colloid group in all patients with burns up to 50 per cent body surface area, but only on the first day after burning. As the extension of the burned area increased, there was a tendency for potassium excretion to increase, but the difference was not statistically significant in either group.

Renal function. Table II lists renal function studies in 17 patients at 24 or 48 hours after commencement of therapy. Unfortunately, the number of patients studied in each therapy group was not sufficiently large for statistical comparison. Nevertheless, it is noteworthy that the saline-treated patients who were young and free from shock demonstrated the same increased glomerular filtration and normal renal plasma flow observed in a group of healthy Peruvian males given a similar sodium load.[19] On the other hand, colloid-treated patients who were not in shock showed normal glomerular filtration but decreased renal plasma flow. Filtration fraction was high in both therapy groups. Patients who were over 60, who suffered from shock, or who had very severe burns showed markedly decreased glomerular filtration and renal plasma flow regardless of therapy.

Sodium excretion during the clearance periods was higher in the saline group than in the colloid group, but the values were much lower than those obtained in healthy individuals given a similar sodium and water load.[19] Potassium excretion was higher in both therapy groups than that seen in healthy subjects.

Fig. 1 illustrates urine output and total sodium and potassium excretion in the saline-treated patients at 2-hour intervals after commencement of saline solution therapy. Compared with normal individuals given the same sodium and water load,[19] the urine flow and total sodium excretion was much less in the burned patients. Pa-

Table II. *Renal function in burned adults*

% burn	Time after burning (hr.)	Patient	Age	Sex	Glomerular filtration (ml./min.)	Renal plasma flow (ml./min.)	Filtration fraction	Urine volume (ml./min.)	Total sodium excretion (mEq./min.)	Total potassium excretion (mEq./min.)	Final outcome
Saline group											
10 to 25											
	24	Y. H.	16	F	156	513	0.3	0.44	0.114	0.035	Discharged well
		F. J.	22	F	182	459	0.4	1.08	0.061	0.057	Discharged well
		R. S.	14	M	124	720	0.2	0.96	0.330	0.039	Discharged well
		G. H.	24	M	191	953	0.2	2.14	0.530	0.108	Discharged well
	48	C. S.	20	F	141	373	0.4	0.50	0.100	0.021	Discharged well
		J. C.	35	M	238	740	0.3	1.30	0.354	0.094	Discharged well
26 to 50											
	24	E. Z.*	73	F	29	167	0.2	0.38	0.009	0.037	Died at 18 days
	48	F. L.	60	F	87	413	0.2	0.72	0.043	0.076	Died at 15 days
		C. C.	18	F	186	838	0.2	0.72	0.046	0.111	Died at 15 days
		M. A.	28	M	190	716	0.3	1.81	0.404	0.077	Discharged well
		T. Z.	38	F	101	357	0.3	0.60	0.047	0.091	Died at 18 days
		A. E.†	24	F	119	511	0.2	1.64	0.040	0.236	Died at 16 days
51 to 75											
	48	T. F.	13	F	24	122	0.2	0.58	0.038	0.034	Died at 18 days
Colloid group											
10 to 25											
	24	S. E.	19	F	103	347	0.3	0.48	0.010	0.056	Discharged well
26 to 50											
	24	C. T.	47	F	90	334	0.3	0.88	0.028	0.115	Discharged well
		F. R.*	24	F	14	45	0.3	0.15	0.004	0.010	Died at 5 days
51 to 75											
	48	A. C.*	17	F	112	281	0.4	3.03	0.061	0.100	Died at 4 days

*Systolic blood pressure during clearance measurements was below 90 mm. Hg.
†Patient was 6 months pregnant.

tients with more severe burns showed less water and sodium output throughout the course of therapy than those with less extensive burns. There were no striking differences in potassium excretion, however, when compared with the severity of the burn or with the excretion of normal individuals.

Plasma volume. Fig. 2 illustrates the 4-sample T-1824 plasma volumes obtained at the time of admission to the hospital or within 12 hours after burning in 34 patients. The average plasma volume varied inversely with body surface area burned up to a 50 per cent surface area burn. Burns above that level showed no commensurate decrease in average plasma volume.

Fig. 3 and Table III illustrate the response of the plasma volume to fluid therapy. In patients with burns of 10 to 25 per cent body surface area, the average plasma volume of both therapy groups returned to within the normal range at 24 hours (Fig. 3), but treatment with saline solution produced a greater percentage of patients with plasma volumes within the normal range at 24 and 48 hours after commencement of therapy (Table III). In patients with burns of 26 to 50 per cent body surface area, the average plasma volume returned within the normal range only after 48 hours (Fig. 3), with the saline-treated patients showing a better restoration of normal volume. Again, a greater percentage of

the patients treated with saline solution had plasma volumes within the normal range at 24 and 48 hours (Table III). This group included one 46-year-old male patient with a 44 per cent burn who was treated with 1,150 ml. of plasma but who died after 31 hours. Seven hours before death, his plasma volume was still 65 per cent of the minimal normal for his weight. In patients with burns of 51 to 100 per cent body surface area, the average plasma volume returned equally well within the normal range in both therapy groups, but only at 48 hours after thermal injury (Fig. 3). At 24 hours, 100 per cent of the patients in both therapy groups had plasma volumes below the minimal normal range, whereas at 48 hours only 1 of the 3 saline-treated patients had a plasma volume below the minimal normal range (Table III). This group included 2 patients who died, both in the colloid group. One was a 26-year-old man with an 86 per cent burn who had a plasma volume 51 per cent of minimal normal on admission and who died at 18 hours even though he had received 1,000 ml. of Lyovac. The other was a 21-year-old man with a 67 per cent burn who had a plasma volume of 65 per cent of minimal normal on admission. The plasma volume rose slightly to 71 per cent of minimal normal at 24 hours, after the administration of 1,000 ml. of plasma, but the patient died at 48 hours even though an additional 500 ml. of plasma had been administered.

Hematocrit. Table IV shows that on the patient's admission to the hospital after thermal trauma, the average hematocrit increased significantly as the burn extension increased. Fig. 4, *A* shows the response of the average hematocrit to therapy at specified time intervals after thermal injury. In patients with burns up to 50 per cent body surface area the saline group showed a lower average hematocrit throughout the course of the shock period compared with patients in the colloid group. At 48 hours after thermal injury, the difference in hematocrit between the two groups was statistically significant. In patients with the more

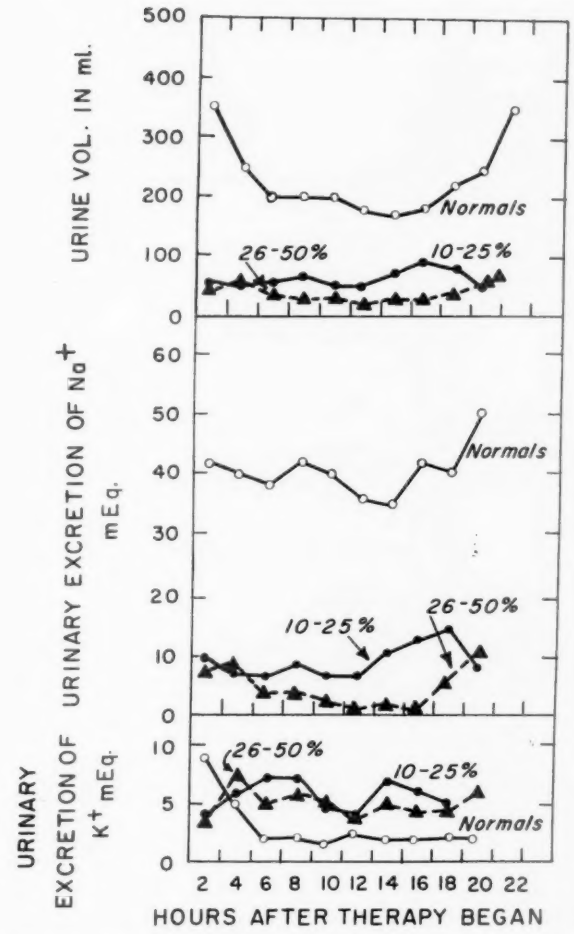

Fig. 1. All burned patients received saline solution exclusively by oral route. The values labeled "normals" were average values obtained from 12 healthy Peruvian males given a similar oral sodium load.[19] All points on burn curves represent average values of 10 patients with 10 to 25 per cent burns and 8 patients with 26 to 50 per cent burns.

Table III. *Per cent of patients with plasma volumes below minimal normal range*

% burn	Therapy group	No. of cases	% of patients with plasma volumes below minimal normal range		
			On admission	At 24 hr.	At 48 hr.
10 to 25	Saline	7	57	14	0
	Colloid	5	80	75	25
26 to 50	Saline	8	88	29	13
	Colloid	5	75	100	50
51 to 100	Saline	4	67	100	33
	Colloid	5	50	100	0

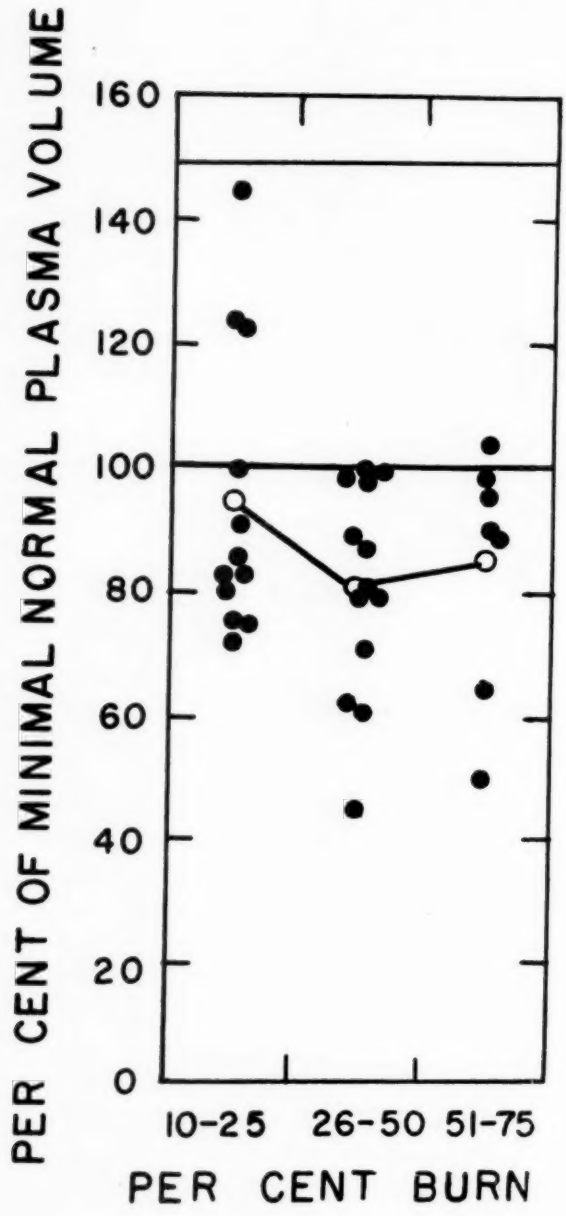

Fig. 2. Minimal normal plasma volume for each patient = [average plasma volume of healthy individuals in ml./Kg. − 2 × standard deviation in ml./Kg.] × the Kg. of body weight of the patient. The average plasma volume for healthy Peruvian males was 42.3 ml. per kilogram (standard deviation = 4.7 ml. per kilogram) and for females 41.4 ml. per kilogram (standard deviation = 4.3 ml. per kilogram). The uninterrupted lines at 100 and 150 per cent of minimal normal values represent the limits of the normal range (average ± 2 × standard deviation). Each point denotes a single case.

extensive burns, the average hematocrit of a small number of patients in both groups was lower in the saline group until 18 hours after thermal injury. Thereafter, there was no major difference between the two.

Total plasma proteins. Table IV shows that there was no significant correlation of total plasma protein before treatment with per cent area burned. Fig. 4, *B* shows the response to therapy at specified time intervals after thermal trauma. In all burns throughout the course of the shock period the average plasma proteins were significantly lower in the patients treated with saline solutions compared with those given plasma supplemented with glucose and water.

Plasma electrolytes. Table IV lists the average initial values of plasma electrolytes at the time of admission to the hospital, while Fig. 5 illustrates the average values during fluid therapy. It is apparent that the initial average values of sodium, potassium, and chloride all fell within the normal range and that there was no significant correlation of these initial values with extension of body area burned (Table IV). The initial average values of bicarbonate, however, fell below the normal range even in patients with 10 to 25 per cent burns, and the average value showed a tendency to decrease as the severity of the burn increased. During therapy the electrolytes of the patients in the saline group were better maintained within the normal range during both postburn days. Table V lists the incidence of electrolyte abnormalities at the termination of the shock period. Whereas the colloid group showed a higher incidence of hyponatremia and hypochloremia after therapy, the saline group showed a greater incidence of hypernatremia, hyperchloremia, and hypokalemia. Both groups showed evidence of a metabolic acidosis (low plasma bicarbonate and blood pH), but the incidence was less in the saline group.

MATERIALS AND METHODS—CHILDREN

The laboratory data in a study of 184 children between the ages of 2 months and

11 years are presented. Only patients with burns of 10 per cent or more of the body surface area are included. Thirty-seven per cent of the children suffered burns from flames, while the rest were from hot fluids. Two separate therapy comparisons have been made in children.

First therapy comparison.[16]

Saline group. Fifty children received orally and/or parenterally a quantity of saline solution of composition similar to that given to adults equivalent to 17 per cent of body weight during the first 48 hours after thermal injury.

Colloid group. Sixty children received during the same time period an average quantity of "colloid" solutions (plasma, blood, and polyvinylpyrrolidone) equivalent to 3.2 per cent of body weight supplemented with a quantity of water orally and/or 5 per cent glucose in water intravenously to equal the total amount of fluid administered to the former group. The quantity of colloid administered is considered "adequate" by most surgeons.[8]

Second therapy comparison.[17]

Saline group. Thirty-four children were treated with isotonic saline solutions orally and/or parenterally in amounts equivalent to 15 per cent of body weight during the first 48 hours after burning.

Saline and plasma group. Fifty children received the same amount of saline solution but with part of the saline solution administered as plasma intravenously in amounts considered to be adequate (3.1 per cent body weight) during the same time period.

Patients were strictly alternated between

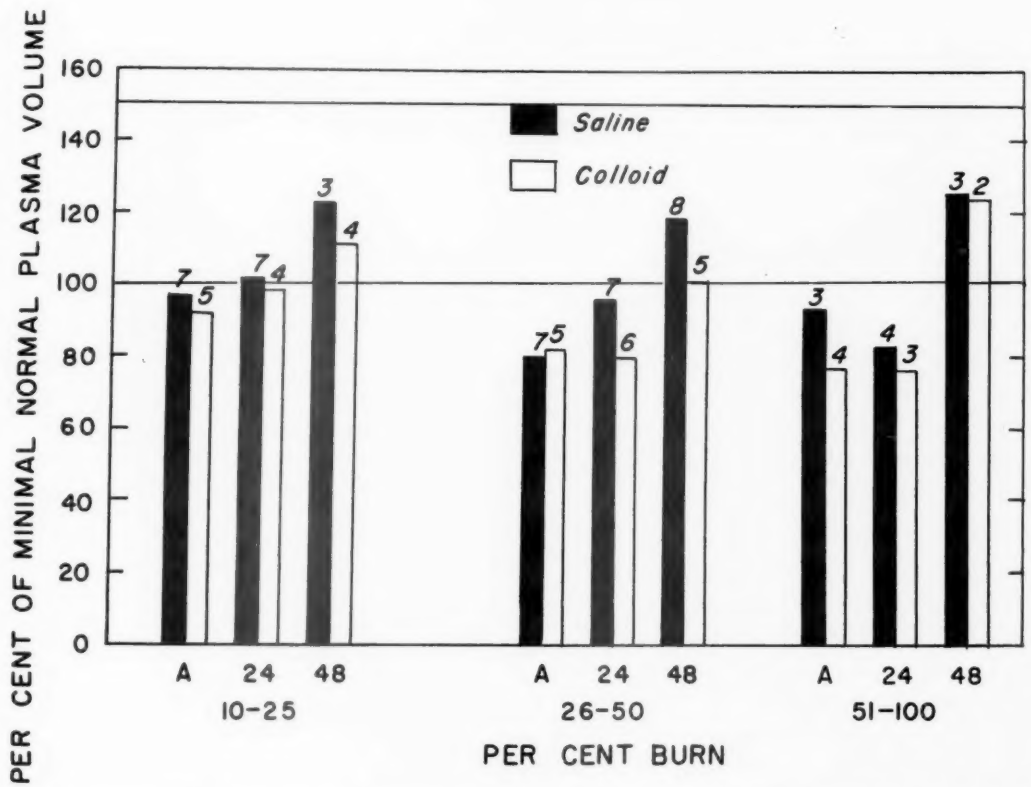

Fig. 3. Minimal normal plasma volume was calculated as described in legend of Fig. 2. The bars represent average values and the numbers above the bars denote the number of cases studied to determine the average value. The uninterrupted lines at 100 per cent (see Fig. 2 for average values) and 150 per cent of minimal normal values represent the limits of the normal range (average ± 2 × standard deviation). On the abscissa, *A* represents the level on admission to hospital, and *24* and *48*, the level at 24 and 48 hours after thermal injury.

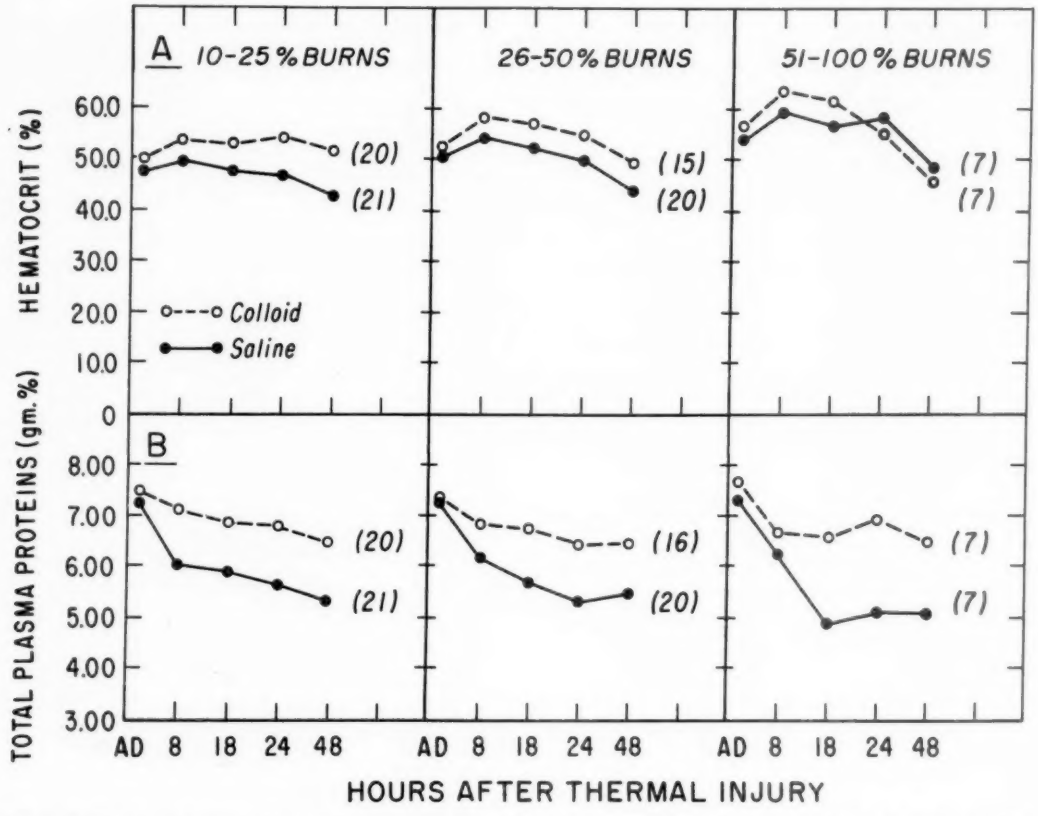

Fig. 4. Each point on the graph represents the average value of the number of patients denoted in parentheses. Only patients with 3 or more measurements taken during the first 24-hour postburn period have been included on the graph. *AD* refers to the value on admission to hospital.

the two therapy groups compared simultaneously. All accessory therapy was identical in the groups compared simultaneously and consisted chiefly of measures routinely employed in hospital practice. In children the local therapy consisted of the exposure method with the application of a sulfanilamide preparation to the burned area during the first therapy comparison mentioned and solely of the exposure method without a local chemotherapeutic agent during the second therapy comparison. Details of these therapy comparisons in children are presented in other reports.[16, 17]

Blood and plasma determinations. The procedure for drawing blood and the time intervals of study were exactly as those described in adults. All of the methods listed for adults apply for childen. No data on water or electrolyte balance could be obtained on the children because of the difficulty in taking quantitative urine collections.

RESULTS IN CHILDREN

The data of the two separate saline groups in children have been combined in the presentation of the results, since both groups were considered to be essentially the same. The absence of statistical difference between the mortality rate and laboratory data of the two saline groups bolstered confidence in the decision to combine them.

The division of children into groups of 10 to 20, 21 to 30, 31 to 40, and 41 to 100 per cent burns, rather than into larger categories as in adults, was done because a burn over 30 per cent body surface area was almost always fatal to a child.

Hematocrit. Table VI shows that on admission to the hospital before com-

Table IV. *Initial laboratory data before treatment of burned adults*

Parameter measured	*% burn*							
	10 to 25		*26 to 50*		*51 to 75*		*76 to 100*	
	No. of cases	*Av. value ± standard deviation*	*No. of cases*	*Av. value ± standard deviation*	*No. of cases*	*Av. value ± standard deviation*	*No. of cases*	*Av. value ± standard deviation*
Hematocrit %	46	49.1 ± 5.7	33	52.7 ± 5.8	12	58.2 ± 7.6	8	60.7 ± 10.6
Total plasma protein (Gm. per cent)	45	7.30 ± 0.49	33	7.32 ± 0.52	12	7.29 ± 0.59	8	7.64 ± 0.39
Plasma electrolytes (mEq./L.)								
Sodium	43	135.6 ± 3.6	33	136.2 ± 4.1	11	136.8 ± 6.2	7	135.8 ± 7.2
Potassium	43	3.83 ± 0.45	35	3.91 ± 0.68	11	4.06 ± 0.60	5	3.43 ± 0.35
Chloride	29	102.9 ± 3.9	32	102.3 ± 4.0	9	101.6 ± 3.8	5	98.5 ± 6.5
Bicarbonate	24	20.8 ± 1.9	25	19.7 ± 2.9	6	18.2 ± 1.87	4	16.7

Table V. *Incidence of electrolyte abnormalities in burned adults at 48 hours after thermal trauma*

Plasma electrolyte	*Therapy group*	*% burn*								
		10 to 25			*26 to 50*			*51 to 100*		
		No. of cases	*% hypo**	*% hyper†*	*No. of cases*	*% hypo**	*% hyper†*	*No. of cases*	*% hypo**	*% hyper†*
Sodium	Saline	24	33	0	18	6	22	9	11	22
	Colloid	22	77	0	15	80	0	7	71	14
Potassium	Saline	24	42	0	19	39	5	9	0	22
	Colloid	23	17	0	17	12	12	6	0	17
Chloride	Saline	17	18	0	18	17	11	7	71	14
	Colloid	13	61	0	16	62	0	6	33	0
Bicarbonate	Saline	19	16	0	15	0	7	6	17	0
	Colloid	12	50	0	12	60	0	6	50	0

*Refers to levels below the normal range.

†Refers to levels above the normal range.

Table VI. *Initial laboratory data before commencement of fluid therapy in burned children*

Parameter measured	*% burn*							
	10 to 20		*21 to 30*		*31 to 40*		*41 to 100*	
	No. of cases	*Av. value ± standard deviation*	*No. of cases*	*Av. value ± standard deviation*	*No. of cases*	*Av. value ± standard deviation*	*No. of cases*	*Av. value ± standard deviation*
Hematocrit per cent	111	42.3 ± 4.2	41	46.2 ± 6.11	12	46.7 ± 3.0	15	52.0 ± 5.5
Total plasma proteins (Gm. per cent)	105	6.91 ± 0.47	40	6.79 ± 0.59	12	6.93 ± 0.54	15	6.89 ± 1.05
Plasma electrolytes (mEq./L.)								
Sodium	97	134.1 ± 3.9	40	134.1 ± 4.3	11	132.8 ± 2.8	11	132.1 ± 6.4
Potassium	91	3.82 ± 0.63	38	3.89 ± 0.64	9	3.43 ± 0.54	11	3.71 ± 0.61
Chloride	76	102.7 ± 3.7	38	102.1 ± 4.9	9	99.1 ± 4.8	9	100.3 ± 2.8
Bicarbonate	54	19.1 ± 2.9	20	16.7 ± 3.8	9	15.7 ± 1.9	3	17.4

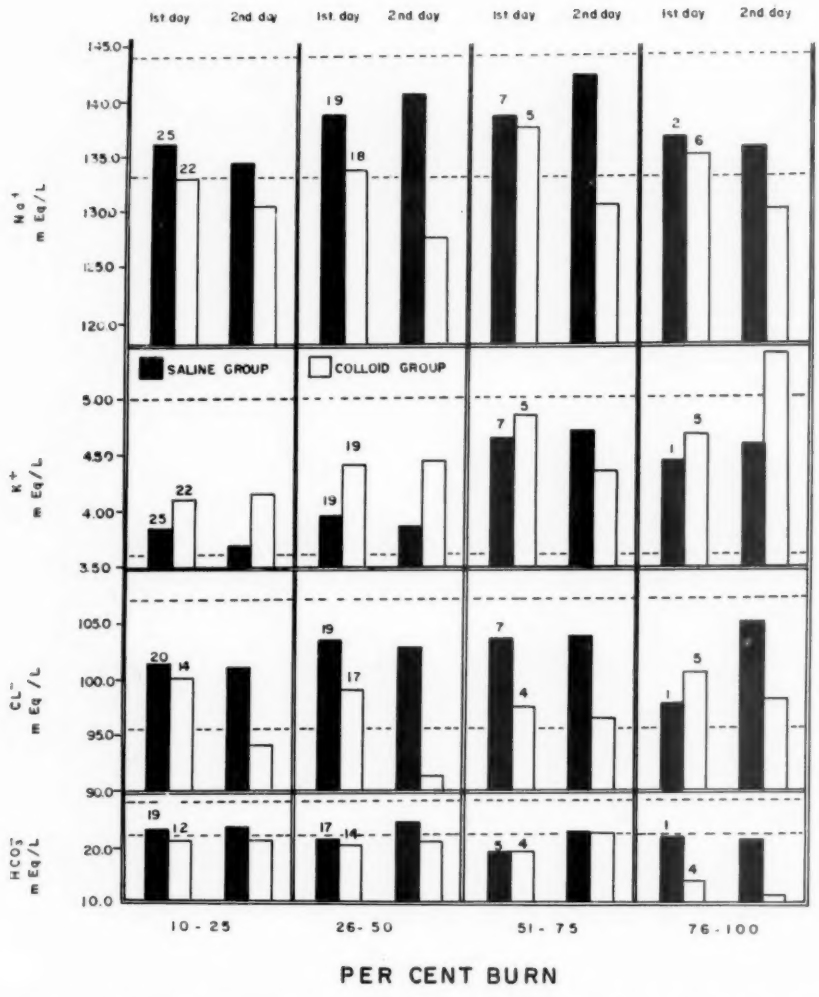

Fig. 5. The bars represent average values, and the numbers above the bars denote the number of cases used in the determination of the average value. The interrupted lines demonstrate the normal range of values, for sodium 133.0 to 144.0 mEq./L., for potassium 3.60 to 5.00 mEq./L., for chloride 95.5 to 106.5 mEq./L., for bicarbonate 22.0 to 27.0 mEq./L.

mencement of fluid therapy, the average hematocrit significantly increased as the burn extension increased. Fig. 6, *A* shows the response of the average hematocrit to therapy at specified time intervals after thermal injury. In patients with burns of 10 to 20 per cent body surface area, there was very little difference between the average hematocrit in the 3 therapy groups until 24 hours after thermal injury, after which time the colloid group showed a significantly higher hematocrit than either the saline or saline and plasma groups. In patients with burns of 21 to 30 per cent body surface area, those treated with colloid showed a higher average hematocrit throughout the shock period than patients in the other 2 groups. In patients with the more severe burns, the saline and plasma group showed a lower average hematocrit during the same time period than either the colloid or saline groups.

Total plasma proteins. Table VI demonstrates that initially there was no significant correlation of total plasma proteins with per cent area burned. Fig. 6, *B* demonstrates the response of the average plasma proteins to therapy at specified time intervals after thermal injury. In all burn patients throughout the course of the shock period, the

average plasma proteins were lower in the patients treated with saline solutions than in the other two groups. In patients with burns up to 30 per cent body surface area, the differences between the saline and either the colloid or saline and plasma groups were statistically significant. On the other hand, the differences in plasma proteins between the colloid and saline and plasma groups did not show statistical significance. In patients with the most severe burns therapy with saline and plasma showed the most effective maintenance of plasma protein levels during the shock period.

Plasma electrolytes. Table VI lists the average initial values of plasma electrolytes after burning. It is evident that the average values of sodium, potassium, and chloride fell within the normal range and that there was no significant correlation of these electrolytes with the per cent area burned. The initial average value of bicarbonate, however, fell below the normal range in all burn groups, and the average value decreased significantly up to 30 per cent body area burned. During therapy the saline and plasma group showed average values that stayed more consistently within the normal range than either of the other two therapy groups (Fig. 7). At the termination of the first 48 hours of therapy, as Table VII indicates, the patients in the colloid group had a higher incidence of hyponatremia, hypochloremia, and hyperkalemia than the other groups, while the other two showed a higher incidence of hypernatremia, hyperchloremia, and hypokalemia than the colloid group. All three groups showed a high incidence of metabolic acidosis, which persisted with fluid therapy.

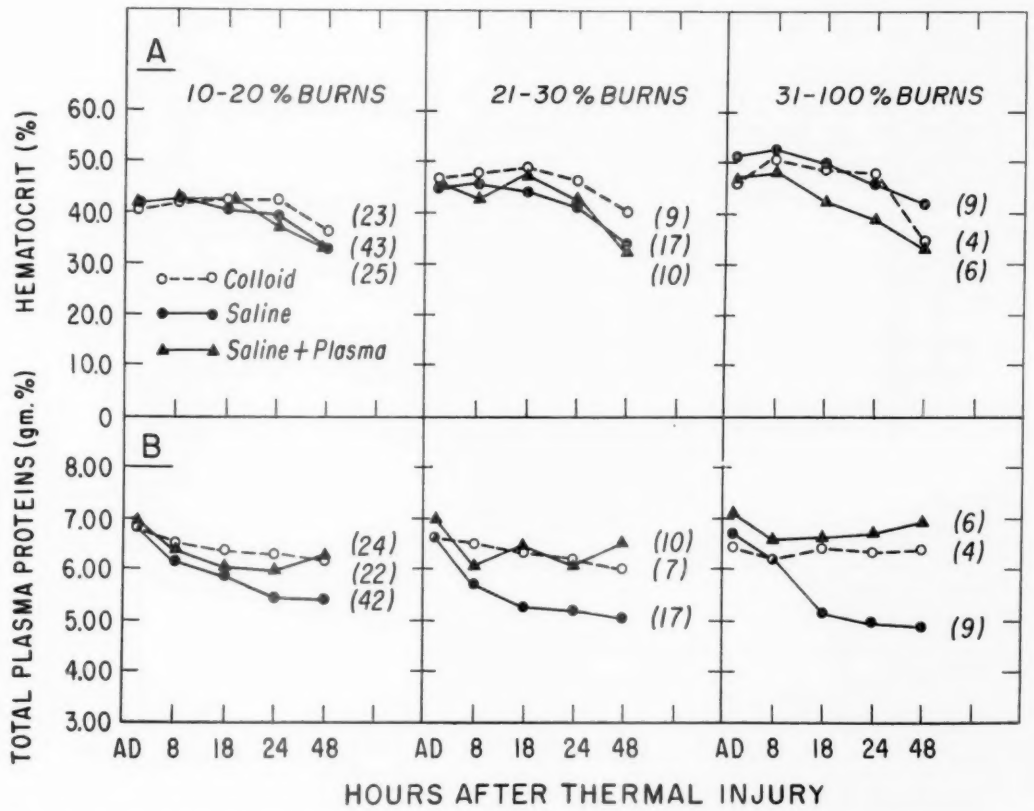

Fig. 6. Each point on the graph represents the average value of the number of patients denoted in parentheses. Only patients with 3 or more measurements taken during the first 24-hour postburn period have been included on the graph. *AD* refers to value on admission to hospital.

Table VII. *Incidence of electrolyte abnormalities in burned children at 48 hours after thermal trauma*

Plasma electrolyte	*Therapy group*	*% burn*								
		10 to 20			*21 to 30*			*31 to 100*		
		No. of cases	*% hypo**	*% hyper†*	*No. of cases*	*% hypo**	*% hyper†*	*No. of cases*	*% hypo**	*% hyper†*
Sodium										
	Saline	48	25	15	17	24	35	6	16	33
	Colloid	27	92	0	8	88	0	6	100	0
	Saline and plasma	27	0	11	11	9	27	7	0	29
Potassium										
	Saline	47	15	19	16	25	6	5	0	80
	Colloid	24	4	46	9	11	56	6	0	50
	Saline and plasma	26	19	12	8	0	25	6	17	33
Chloride										
	Saline	37	16	5	12	33	25	4	0	50
	Colloid	16	77	0	7	86	0	5	100	0
	Saline and plasma	23	4	10	10	10	10	6	17	33
Bicarbonate										
	Saline	23	83	0	7	86	0	5	80	0
	Colloid	13	69	0	4	0	0	5	80	0
	Saline and plasma	26	96	0	9	45	0	6	67	0

*Refers to levels below the normal range.

†Refers to levels above the normal range.

DISCUSSION

Our knowledge of the course of physiologic events consequent to trauma has evolved from the mass of experimental work in animals and in man performed during the past 4 decades. Yet, in a search through the literature, it is often surprising to note the relative paucity in the number of burned patients studied. Even if these numbers are sufficient in themselves to reflect the changes due to thermal trauma in man, there is, nevertheless, a real lack of information on the effect of administered fluid therapy in man upon the circulation and fluid and electrolyte balance. It is for that reason that the data presented here are believed to be valuable, since a large number of burned adults and children have been studied in whom simultaneous comparisons are made with different fluid regimens administered on an alternate case basis.

The decrease in plasma volume and the hemoconcentration that occur after thermal trauma noted by previous investigators[6, 10, 22, 25] are confirmed here. The inverse correlation of initial plasma volume with body surface area burned as reported first by Noble and Gregerson[22] was observed in adults with up to 50 per cent body surface area burned. There was no good evidence of a progressive diminution of plasma volume in patients with the more severe burns. Measurements of the extracellular fluid volume with thiocyanate demonstrated a progressive expansion of that fluid compartment in patients with burns involving up to 50 per cent of the body surface area; patients with more severe burns showed no further expansion.[6] On the other hand, hardly any previous work has been carried out in human beings concerning the effect of therapy during the shock period upon plasma volume.[10] Our data in adults indicate that saline solutions were more effective in restoring the plasma volume to within the normal range than treatment with inadequate electrolyte and protein. Hemoconcentration in both adults and children during the first day after burning was also more effectively diminished by therapy with

saline solutions than with plasma and water.

In adults the retention of fluid and sodium described by others[5, 21] was noted only in the patients given large quantities of sodium. Adult patients given plasma and water (containing only small amounts of sodium) showed no over-all water or sodium retention. In the adult saline-treated patients there was no significant increase in fluid retention as the extension of the burned area increased, but there was a significant increase of fluid lost locally into the bed sheets (as demonstrated by the data on calculated extrarenal losses) and a significant diminution of urinary volume in patients with the more severe burns. Sodium balance became increasingly more positive as the extension of the burn increased in the group that received saline solutions, whereas sodium balance was negative in all patients treated with plasma and water. Daily urinary sodium excretion in both therapy groups decreased as the burn became more extensive, while the sodium excretion of the saline-treated patients was significantly higher than in the group who received little sodium. Renal sodium excretion in the saline-treated patients was not as high, however, as that in a group of healthy individuals given a similar sodium and water load.[19]

As has been noted by others, a negative

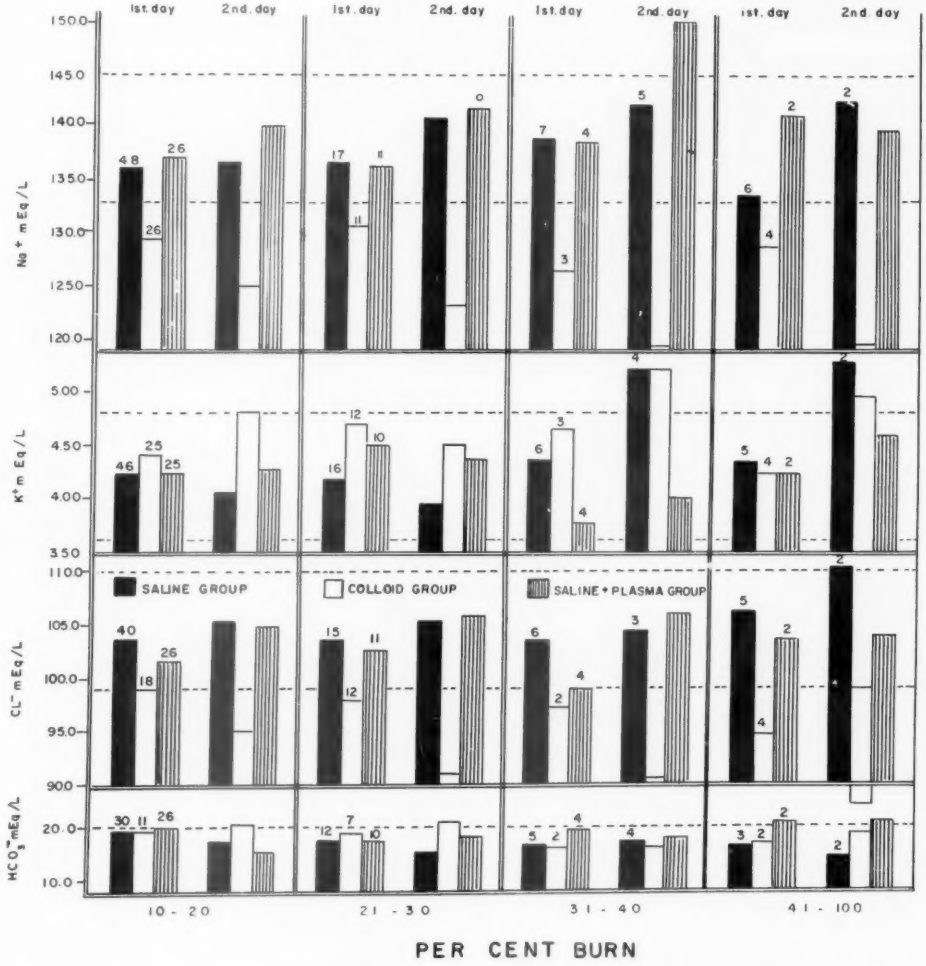

Fig. 7. The bars represent average values, and the numbers above the bars denote the number of cases used in the determination of average value. The interrupted lines demonstrate the normal range of values, for sodium 133.0 to 145.0 mEq./L., for potassium 3.60 to 4.80 mEq./L., for chloride 99.0 to 110.0 mEq./L., for bicarbonate 20.0 to 25.0 mEq./L.

potassium balance was observed in adults of both therapy groups. The saline group demonstrated a significantly higher urinary potassium excretion than the colloid group, but only on the first day of therapy. No significant increase in potassium excretion could be detected in either group as the burn area increased.

Only 3 or 4 burn cases have been reported in which renal hemodynamics have been studied during the shock period.[13, 15] In the present report no initial measurements were made immediately after burning because of the difficulty in getting adequate urinary flow. Measurements taken after therapy had begun were obtained at 24 and 48 hours after burning. Adult patients who were in shock or who had very severe burns showed decreased renal plasma flow and glomerular filtration, as could be expected.[15] Young adult patients treated with saline solutions demonstrated increased glomerular filtration and normal renal plasma flow with an elevated filtration fraction. The patients who received plasma and water showed normal glomerular filtration and slightly decreased renal plasma flow with an increased filtration fraction. These data are in accord with the data on the few burn patients studied previously as well as data on healthy individuals given a similar sodium load.

Reports in the literature vary in the concentration of total plasma proteins observed in burned patients.[3, 6] Our data show no evidence of increased average levels initially even after severe burns in adults or children. With therapy, plasma proteins dropped to varying degrees, but patients who received adequate protein therapy for the most part maintained total plasma protein levels closer to the normal range. Both adults and children who received saline solutions exclusively, however, showed markedly decreased levels during therapy. This phenomenon was apparently without bad effect initially, since there were no deaths in adult patients during the first 60-hour postburn period.[17]

Hyponatremia and metabolic acidosis are the most characteristic electrolyte disturbances reported by others.[3, 5, 8, 25] Initial electrolyte values in adults and children of Peru usually demonstrated no deviation from normal except for lowered plasma bicarbonate values. With therapy, the patients who received little sodium replacement therapy showed a high incidence of hyponatremia and hypochloremia. Hyperkalemia was more prominent in patients with the more extensive burns with a higher incidence evident in those receiving little sodium. The saline-treated adults and children demonstrated a higher incidence of hypernatremia, hyperchloremia, and hypokalemia. In adults the incidence of metabolic acidosis during therapy was appreciably less in the saline-treated patients, but no such effect was seen in children.

Since there was a zero 60-hour mortality rate during therapy of the saline-treated adults, it is tempting to conclude that the physiologic changes brought about by saline solution therapy were responsible for survival. To be sure of this conclusion, however, it would be necessary to analyze statistically differences of patients who lived and died. This was done for hematocrit, total plasma proteins, and plasma sodium, but no significance for survival could be found in those differences in adults of the colloid group or children of all therapy groups. Response of plasma volume to therapy might be a better therapeutic index, but insufficient data have been collected to analyze the results statistically. Therefore, as yet there is no current laboratory measurement which can accurately predict survival or death.

SUMMARY

This report presents various laboratory measurements taken during the first 48 hours after thermal injury on a series of 153 adults and 185 children from Peru with burns involving 10 per cent or more of the body surface area. The effect of fluid therapy upon changes in the circulation and fluid and electrolyte balance was assessed by simultaneous comparison of groups of patients to whom different types of fluids

were administered. The fluid regimens employed consisted essentially of one type containing large amounts of sodium with or without added protein and another type with only small quantities of sodium but with varying quantities of protein.

Measurements made soon after thermal trauma but before fluid therapy had been started demonstrated (1) a decreased plasma volume in adults which was proportional to the area burned only in patients with up to 50 per cent of the body surface area involved, (2) hemoconcentration in adults and children proportional to the area burned, and (3) plasma levels of proteins, sodium, potassium, and chloride in adults and children more or less within the normal range with no changes correlated with the extent of the burn. Only plasma bicarbonate was decreased with a trend to lower values in patients with the more severe burns.

Fluid therapy with large quantities of sodium in adults produced over-all fluid and sodium retention with better restoration of plasma volume to normal during the shock period. Glomerular filtration was increased and renal plasma flow normal in patients who were not in shock at the time of the determination. Hemoconcentration in adults and children was quickly corrected, and plasma electrolytes, for the most part, were maintained within the normal range. Total plasma proteins dropped markedly during the early postburn therapy period from the initial value.

On the other hand, fluid therapy with plasma but with only small quantities of sodium in adults produced no over-all water or sodium retention. There was less efficient restoration of plasma volume. The patients who died were included in this therapy group, and their plasma volumes at various times during the shock period were always markedly diminished. Glomerular filtration was normal, but renal plasma flow was decreased in the few patients not in shock. Hemoconcentration in adults and children was more persistent, and a high incidence of hyponatremia and hypochloremia was noted. Total plasma proteins remained fairly close to the normal range.

From this data it is possible to conclude that the composition of the fluid therapy administered during the shock period does indeed influence the response of the circulation and fluid and electrolyte balance. In adults, therapy with large quantities of sodium was more effective in preventing death during the shock period than therapy with plasma supplemented by glucose and water. The less favorable response in the plasma group was most likely due to the low sodium content of the fluid administered to that group. The saline-treated patients also showed better restoration of the circulation and fluid and electrolyte balance. Statistical analysis of the differences in hematocrit, plasma proteins, and plasma sodium of the patients who lived or died, however, did not demonstrate any significant difference by which survival or death could be predicted.

The authors wish to express their gratitude to Dr. Sanford M. Rosenthal, Chief of the Laboratory of Pharmacology and Toxicology, National Institute of Arthritis and Metabolic Diseases, and to Mr. Jacob Lieberman, Statistician of the National Institutes of Health, for their helpful advice on various aspects of this report.

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The recognition of preclinical femoral hernia

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Increasing success has attended the progressive reparative methods that have been employed for various types of inguinal and incisional hernias. The only exception is the continued high mortality rate associated with strangulated femoral hernia. Fortunately, death is seldom attributable to shortcomings of the reparative technique, but is due to delay in the establishment of an accurate diagnosis. Diagnostic procrastination too often results in serious and irreversible complications which may supervene before surgical intervention.[3, 6] It therefore follows that greater emphasis should be placed on the means of making an earlier diagnosis, preferably in the hernia's incipiency, and on repair at that time. Adherence to this principle would obviate the possibility of subsequent strangulation. Moreover, if this ideal objective could be attained it would be a substantial step toward lowering the alarming fatality rate of strangulated femoral hernia. To this end, we propose a new concept for the recognition of preclinical femoral hernia during a varying period before it becomes clinically manifest.

Femoral hernia may be classified into 3 sequential types, (1) preclinical, (2) reducible, and (3) incarcerated. Since textbooks of surgery and the literature have thoroughly acquainted the profession with the latter two types of femoral hernia, the discussion will be limited to ways of augmenting the recognition of preclinical femoral hernia. There seem to be valid grounds based upon anatomic, clinical, and statistical information for the postulation of a diagnosis of preclinical femoral hernia in certain patients undergoing inguinal hernia repair.

Received for publication June 23, 1960.

ANATOMIC PREREQUISITES

There are several anatomic variants which contrive to produce a femoral hernia. Most important for consideration are the dimensional changes of the femoral ring and fovea. It is not practicable because of the interligamentous location of the ring to make accurate measurements. A small ring is recognized by the fact it will not permit engagement of the index finger of the surgeon. A ring of this size practically precludes the subsequent development of a femoral hernia. A normal femoral ring should permit introduction of the tip of the finger, provided that the fovea is deep (Fig. 1). It is the latter component of a ring of normal size that makes it vulnerable. However, if the fovea of such a ring is shallow and the canalicular tissue dense, the tip of the finger will not engage in it (Fig. 2). Such a fovea constitutes a barrier to the development of a hernia. Not infrequently one encounters an incarcerated femoral hernia in an otherwise normal ring which has a deep, incompetent fovea. The paucity of clinical findings almost precludes diagnosis in this stage of incipiency. Perhaps some experience is required to determine a vulnerable versus nonvulnerable ring, but the surgeon who performs a hernia repair

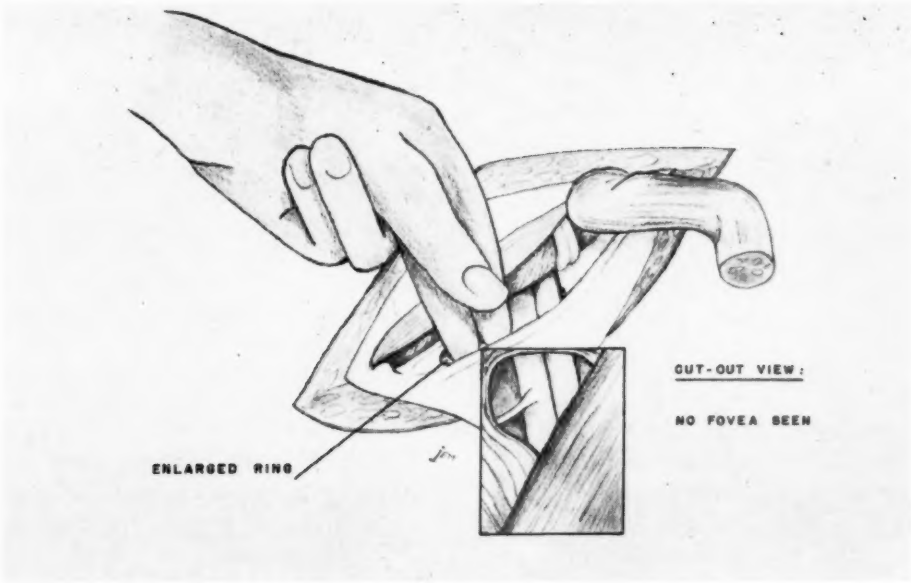

Fig. 1. A normal femoral ring and a deep fovea.

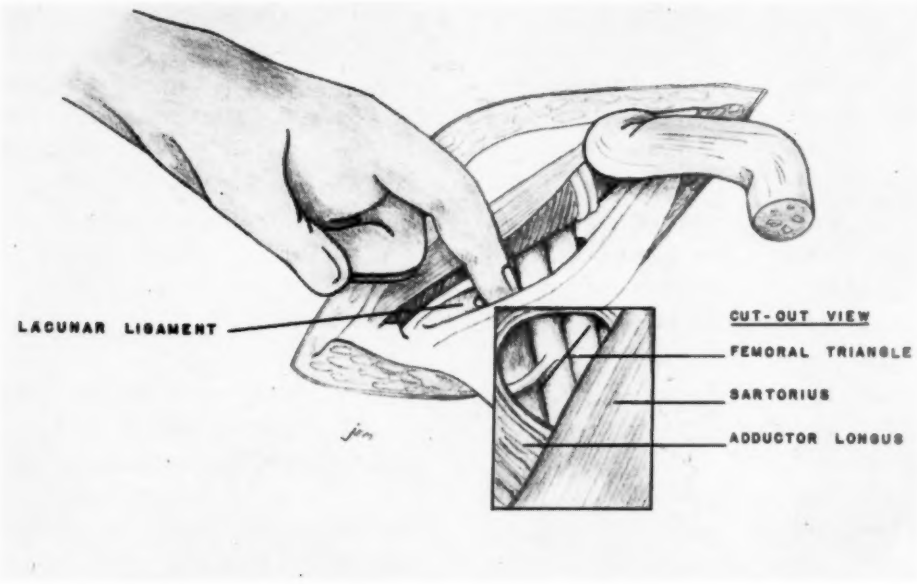

Fig. 2. A normal femoral ring and shallow fovea.

almost daily soon develops clinical acumen. The third type of ring is the large one which is easily recognized (Figs. 3, 4, and 5). It obviously falls within the potential herniation group. Again it should be emphasized that the depth and resistance of the foveal component are as important as the dimensions of the femoral ring.

The ligamentous boundaries, the integrity of the fascia transversalis, and the direction of the femoral ring all play a role in the etiology of preclinical femoral hernia. The medial lacunar ligament is the most vulnerable ligament. Any anteroposterior shortening or increased pliability of its lateral margin predisposes to medial expansion of

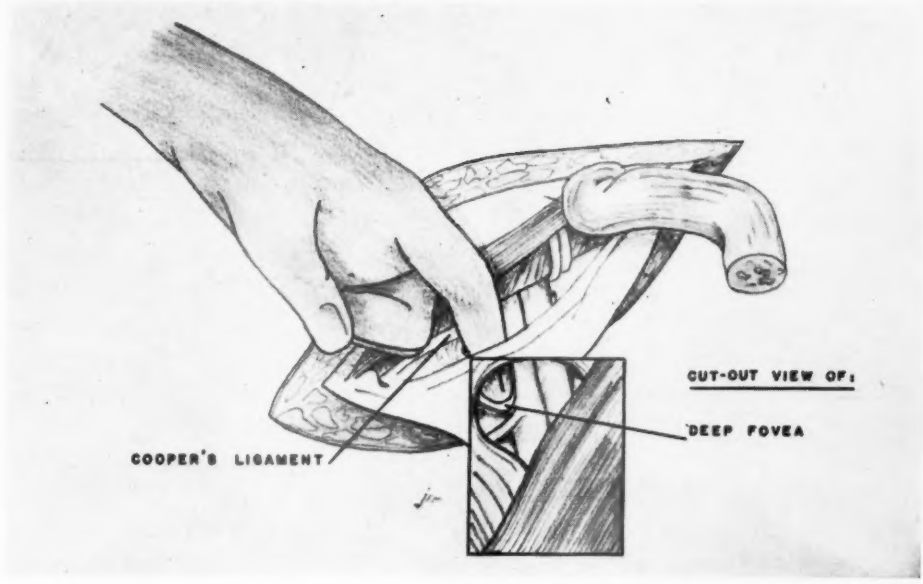

Fig. 3. An enlarged femoral ring and shallow fovea.

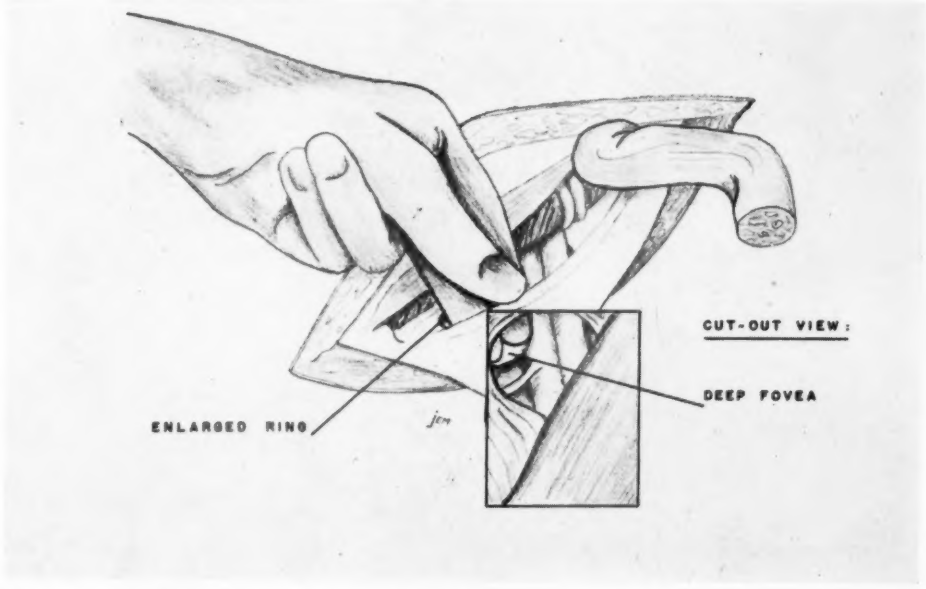

Fig. 4. An enlarged femoral ring and deep fovea.

the femoral ring. A narrowed insertion of the fascia transversalis into the superior pubic ramus, as has been pointed out by McVay and Anson,[8] is often overlooked. When this variant obtains, it exposes the femoral ring directly to intra-abdominal pressure without the buffering action of a normally resistant stratum. The more frequently encountered deficiency is the attenuation of this stratum.

The direction of the femoral ring is horizontal in contrast to the obliquity of the internal and external inguinal rings. The absence of surrounding muscular strata further deprives the femoral ring of elastic recoil which serves as collateral defense to

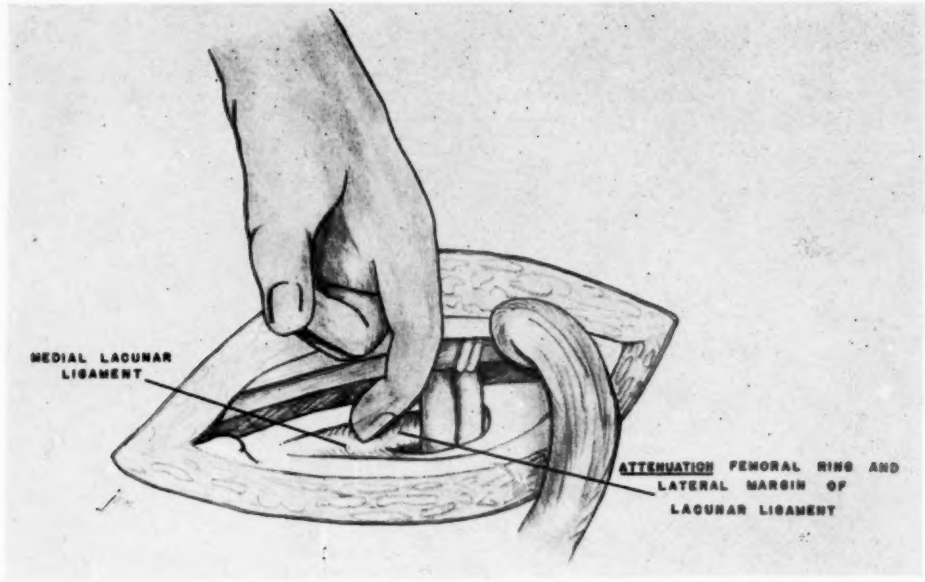

Fig. 5. Deficient lateral margin of lacunar ligament.

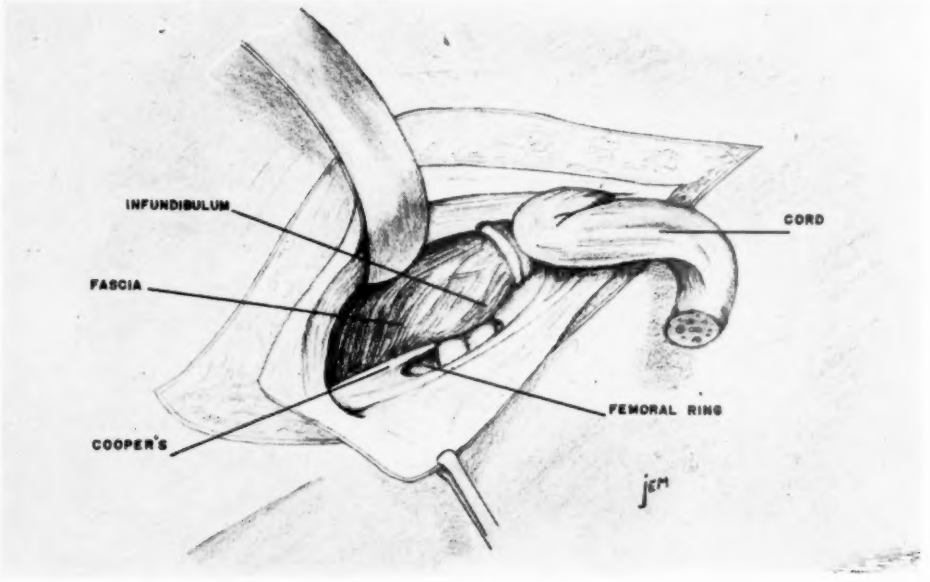

Fig. 6. Normal fascia transversalis and peritoneal infundibulum.

any oncoming intra-abdominal pressure on the inguinal rings. The intrinsic dimensional variations of the femoral ring and the deficiencies of adjacent structures contrive to produce the pre-existing weakness of the femoral area. The vulnerability index of the femoral region is determined by (1) the size and resistance of the boundaries of the femoral ring, (2) the competency of the floor of the femoral fovea, (3) the integrity of the fascia transversalis and obliquus internus muscle, and (4) the ductility of the peritoneal infundibulum.

Clinical data were collected on patients who demonstrated at operation for inguinal hernia sufficient anatomic criteria for a Cooper's ligament repair, but who showed no clinically demonstrable femoral weakness.

In our series of 113 Cooper's ligament repairs of inguinal hernia there were 20 patients (17.6 per cent) in whom the femoral ring and/or fovea were of sufficient size or depth to permit engagement of the tip of the index finger.[1] With completely exposed Cooper's ligament and interligamentous space, the palpatory findings were verified by direct visualization. Even though no peritoneal sac had descended into the ring, the dimensions of the femoral ring were considered sufficient to indicate the existence of a preclinical femoral hernia and a potential source of an incipient femoral hernia. Therefore, in patients who demonstrated these coexisting anatomic features the femoral ring was excluded by means of a Cooper's ligament repair.

CLINICAL PREDISPOSING FACTORS

The peritoneal sac of a femoral hernia arises from the peritoneal infundibulum in the lateral transitional area of the inguinal region. Normally an infundibulum of peritoneum is not recognizable (Fig. 6). However, with functional insufficiency of the transversus abdominis and obliquus internus muscles and with concomitant attenuation of fascia transversalis, slight bulging of the peritoneum becomes recognizable (Fig. 7). At first, it is simply the source of a direct hernial sac, but in time and with continuing intra-abdominal pressure the ductile peritoneum steadily descends and comes to lie over the femoral ring. If this ring is vulnerable, a knuckle of peritoneum may enter it. This sequential peritoneal relationship explains the frequency of the coexistence of direct and femoral sacs.

In patients in whom no femoral hernia has been demonstrable clinically, the presence of a large direct hernial sac should immediately arouse the suspicion that an incipient femoral sac may be present and must be searched for thoroughly. It also follows that when the surgeon is confronted with these cumulative clues a meticulous search should be made for any collateral weakness of the posterior wall of the inguinal canal.

A femoral sac, like that of a direct inguinal hernia, is acquired. This is in contrast to the congenital vaginal process of peritoneum which constitutes an indirect hernia. However, a femoral hernia in its evolutional development does have a congenital component, but the latter is limited to its mural

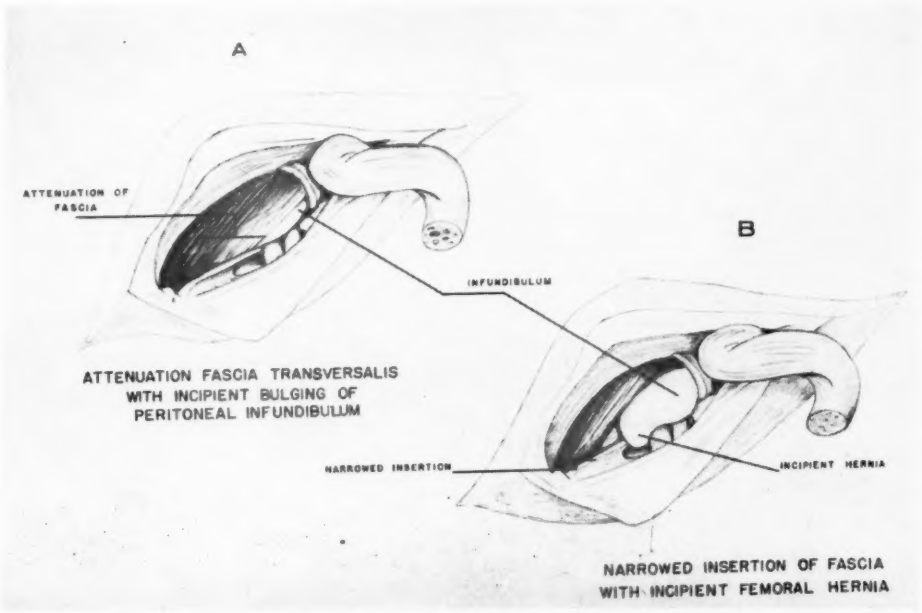

Fig. 7. *A,* Incipient, nonclinical bulging of peritoneal infundibulum. *B,* Incipient femoral hernia.

and ligamentous components. The adjacent fascial weaknesses may be either congenital or may be attributable to the aging process. Krieg, through his diligent clinical observations, has recorded changes due to senescence which he found to involve chiefly the obliquus internus muscle in the older patient. He has not observed similar changes in children or young adults. It is therefore important to know when one is referring to the congenital origin of a hernia whether one is thinking in terms of its saccular origin or in terms of the contribution of the fascial component of the hernia. Less often, dual etiologic factors may exist. In such instances, it may be difficult to determine the predominant one and the problem must be resolved on the basis of composite evaluation of all anatomic elements of the inguinofemoral region.

STATISTICAL DATA

Certain statistical facts regarding femoral hernia are of collateral value in establishing diagnostic leads in equivocal cases. For instance, femoral hernia occurs in persons 40 years of age or more,[4] whereas indirect inguinal hernia is noted in younger individuals. Approximately 25 per cent of all femoral hernias occur in patients who have had inguinal hernia repairs.[2, 7] In our own patients in whom Cooper's ligament repairs were performed for clinically recognizable inguinal hernia, there were structural deficiencies in 17 per cent which could be reasonably accepted as predispositional to the development of femoral hernia. The close anatomic relationship of direct inguinal and femoral hernia invariably creates circumstantial suspicion that the patient is susceptible to the ultimate development of a femoral hernia. The surgeon, on opening the abdomen, is obligated to evaluate all intra-abdominal findings. There should be like responsibility when the surgeon exposes the inguinal canal. If this were done routinely many preclinical hernias could be discovered and proper corrective measures would be taken at that time.

CONCLUSIONS

1. Certain predictive features of preclinical femoral hernia may be recognized during an initial repair of an inguinal hernia.

2. The anatomic variants of a potential femoral hernia are (1) size of the femoral ring and the depth of the fovea, (2) deficiency of the medial lacunar ligament, (3) narrowed insertion of the fascia transversalis into the superior pubic ramus and/or its attenuation, and (4) a discernible peritoneal infundibulum at the lateral transitional angle of the inguinal region, particularly the presence of a direct bulging.

3. The older patient is more prone to develop femoral hernia.

4. A proper perspective of the anatomic, clinical, and statistical factors is essential in determining the existence of a preclinical femoral hernia.

5. The elements contributing to the vulnerability index of the femoral ring have been discussed.

6. The proposed concept of the recognition of preclinical femoral hernia should materially lower the incidence of manifest femoral hernia and ultimately reduce the number of strangulated femoral hernias.

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Internal hernia after gastrojejunostomy

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Construction of each gastrojejunostomy, either as a procedure by itself or as a step in the performance of a partial gastrectomy, results in the formation of an internal hernial ring which may be the cause of severe difficulties in the immediate or distant postoperative period. It is the purpose of this paper to review the anatomic relationships of this internal hernia and to examine critically the world literature concerning the clinical manifestations of this unusual postoperative complication. All available reports have been examined and analyzed. In addition to the reported cases in the literature, 6 case histories of patients manifesting this complication have been included. Five were found in the files of the Columbia-Presbyterian Medical Center and 1 was from the Francis Delafield Hospital. One of the case histories from the Presbyterian Hospital series was reported by McAllister[24] in 1948, but the others have not been published previously.

In all, 92 case histories have been collected and analyzed for presentation. Information concerning the details of the original operation and findings at a second operation or autopsy was often found to be scanty, but an attempt was made to include all applicable clinical and anatomic information.

ANATOMY

The presence of a space of limited area posterior to either a retrocolic or antecolic gastrojejunostomy can be demonstrated unequivocally in the anatomy as seen at operation or autopsy. Moreover a space bounded by structures of limited elasticity is, by definition, an actual or potential hernial ring.

The space which is seen posterior to the retrocolic gastrojejunostomy after partial gastrectomy has for an anterior border the gastrojejunostomy and the afferent limb of jejunum. The superior border is formed by the transverse mesocolon and a small portion of the gastric pouch. The ligament of Treitz forms the inferior border, while the posterior parietal peritoneum is the unyielding posterior wall of the hernial ring (Fig. 1).

In the antecolic gastrojejunostomy after partial gastrectomy, the hernial ring is formed anteriorly by the afferent loop of jejunum and the gastrojejunostomy, superiorly by the transverse colon and the gastrojejunostomy, posteriorly by the transverse colon and transverse mesocolon, and inferiorly by the ligament of Treitz (Fig. 2). There are several unique anatomic circumstances present when there is herniation of the afferent loop in the antecolic gastrojejunostomy which will be described in detail.

Instances of internal herniation after gastrojejunostomy and complementary jejunojejunostomy, which is called Braun's anastomosis in the German literature, have not been included in this paper because such anastomoses are not used routinely today.

Received for publication May 31, 1960.

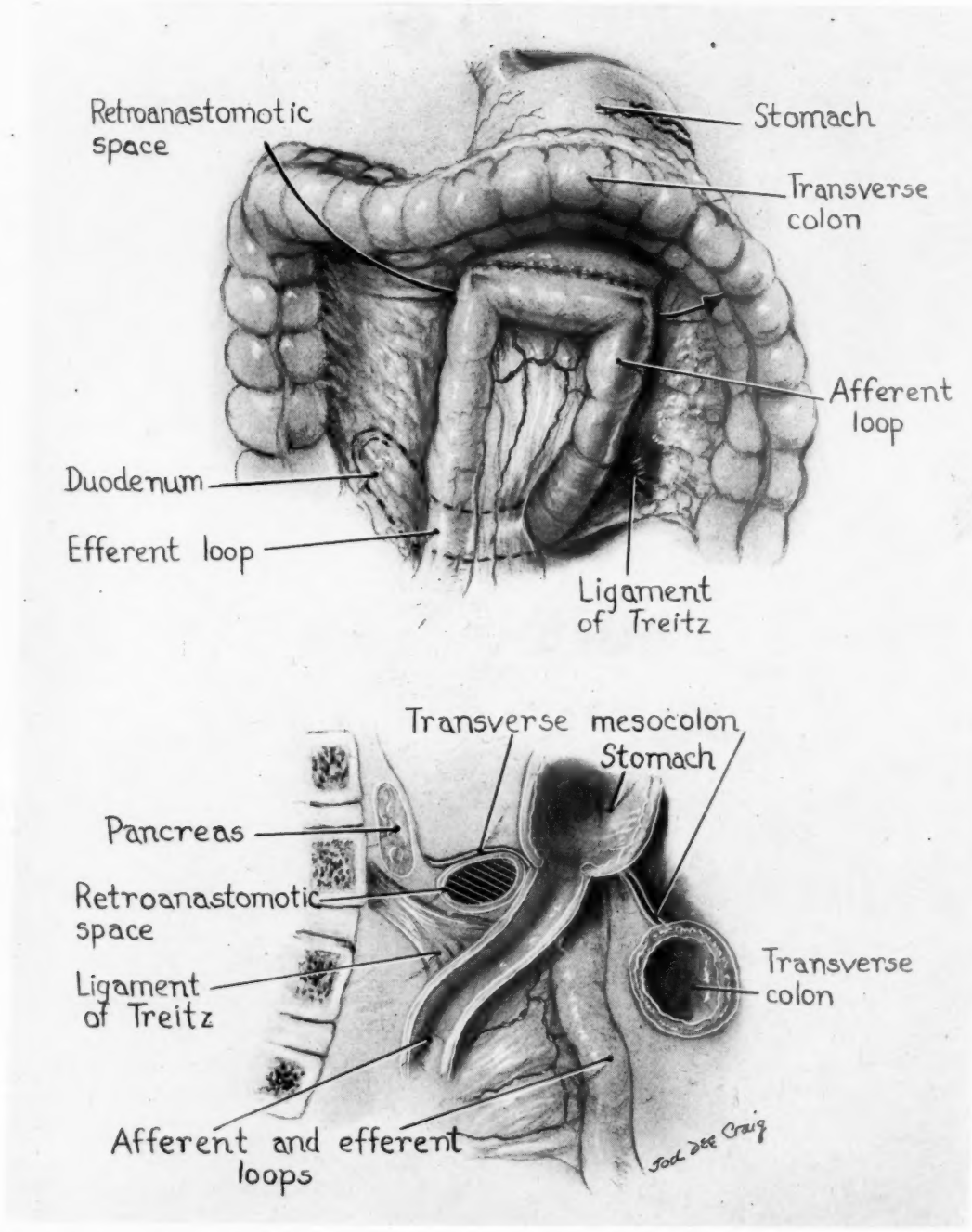

Fig. 1. Frontal and lateral views of the retroanastomotic hernial ring in the retrocolic gastrojejunostomy.

Himmelmann[18] collected many reports of these cases and published them in 1933.

HISTORICAL SURVEY

Credit is usually given to Petersen[40] for being the first to describe the internal hernia. Indeed, herniation of the bowel behind a gastrojejunostomy is occasionally described as "Petersen's hernia."[24, 57] Included in Petersen's original paper, however, is a case history which had been reported by Steudel[48] in 1899. Chlumskij,[10] in a comprehensive dissertation on gastroenterostomy in 1898, predicted that such an internal hernia could give rise to difficulties, but he himself did not know of an actual clinical

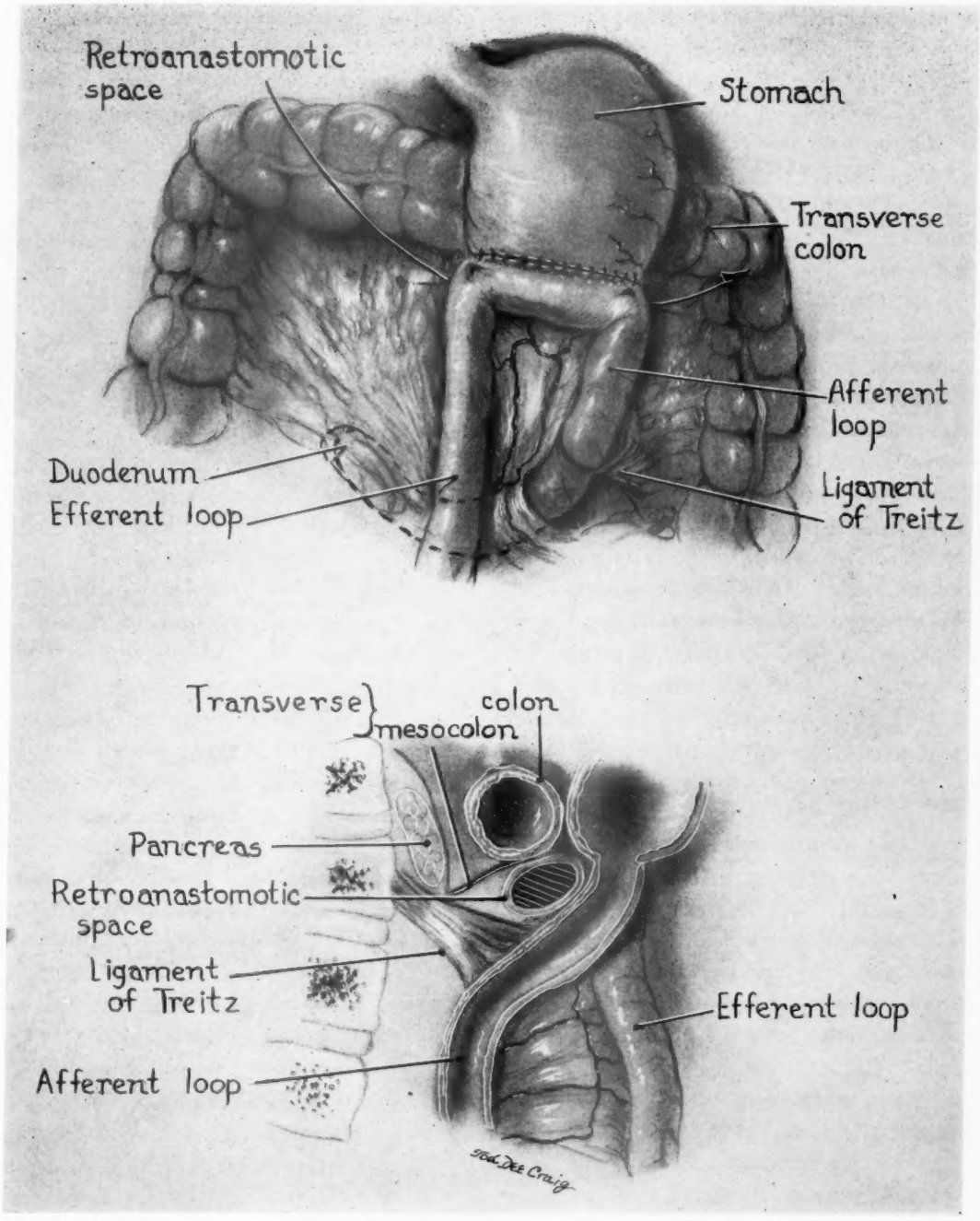

Fig. 2. Frontal and lateral views of the retroanastomotic hernial ring in the antecolic gastrojejunostomy.

example of the complication. It appears that Chlumskij was unaware of a short report of Buddee[7] that had appeared in 1897 which described such an internal hernia after a gastrojejunostomy. Buddee's report was probably the first description of the internal hernia. To Petersen, however, belongs the credit for calling attention to the doleful effects of such a hernia, and it was he who described in detail the first case of this complication following partial gastrectomy and gastrojejunostomy. The earlier reports of Buddee and Steudel concerned the internal herniation of the small bowel after gastrojejunostomy without gastrectomy.

Petersen's contribution was the basis for

recognition of the possibility of an internal hernia behind a gastrojejunostomy in the German surgical literature. Stich and Makkas'[49] textbook of surgery printed in 1958 includes copies of Petersen's original illustrations which had been published 58 years earlier.

The first description in English of the internal hernia was published by W. J. Mayo[28] in 1902. To Mayo also goes the credit for establishing the diagnosis of the hernia at operation rather than at autopsy. By successfully operating upon his patient, Mayo obtained the first survivor of this complication. Soon after publication of Mayo's report, papers by Gray,[17] Barker,[2] and Gordon[16] in Great Britain described isolated instances of the internal hernia as a postoperative complication. In the ensuing years until the present, solitary case reports or small series of them have appeared in the surgical literature throughout the world, that is, wherever gastrectomies and gastrojejunostomies have been performed.

ANALYSIS

The data from the case reports of 92 patients were examined to determine if any correlation could be obtained between the variables in gastrojejunostomy with and without partial gastrectomy and the incidence of internal hernia. The most important variables are: (1) antecolic or retrocolic anastomosis, (2) direction of the jejunal limb in relation to the stomach or gastric pouch, and (3) length of afferent loop.

Antecolic versus retrocolic anastomosis. Examination of the collected case histories shows that internal hernia behind a gastrojejunostomy occurred in 62 patients in whom gastrojejunostomy followed partial gastrectomy and in 30 patients in whom gastrojejunostomy alone was performed. As one might expect, most of the reports of this hernia after gastrojejunostomy alone appeared during the early part of this century when partial gastrectomy was a rather rare operation. As can be seen in Table I, internal hernia appeared somewhat more frequently in patients with partial gastrectomy and antecolic gastrojejunostomy than in patients with a retrocolic anastomosis. However, when gastrojejunostomy alone was performed 87 per cent of the reported cases of internal hernia followed the retrocolic type of operation.

It is probable that these figures do not represent true differences in the propensity of internal herniation to occur after retrocolic gastrojejunostomy, but rather reflect a difference in the incidence with which these anastomoses are performed in various clinics throughout the world.

Direction of jejunal loop. Review of the case reports to determine the direction of the anastomotic loop presented a difficult problem because of the scarcity of information and the ambiguity of the nomenclature. In the gastrojejunostomy without partial gastrectomy, the terms isoperistaltic and antiperistaltic will be used to describe the anastomotic arrangement. Isoperistaltic is defined as that anastomotic arrangement in which the direction of jejunal peristalsis is the same as in the intact stomach, that is, from left to right. Conversely, antiperistaltic refers to that anastomotic arrangement in which jejunal peristalsis is opposite to that of the stomach, or right to left.

The data are summarized in Table II. Again, because of the small number of cases in which adequate information was available, no definite conclusions can be drawn. It may be noted that internal hernia appears to occur more frequently in isoperistaltic gastrojejunostomies than in the antiperistal-

Table I. *Incidence of internal hernia after antecolic and retrocolic gastrojejunostomy with and without partial gastrectomy*

	Antecolic		*Retrocolic*	
	No.	*%*	*No.*	*%*
Gastrojejunostomy with partial gastrectomy (62 patients)	38	61	24	39
Gastrojejunostomy without partial gastrectomy (30 patients)	4	13	26	87

Table II. *Influence of the direction of anastomosis upon the incidence of internal hernia in gastrojejunostomy without gastrectomy*

	Iso-peristaltic	*Anti-peristaltic*	*Not stated*
Antecolic	1 patient	0	3 patients
Retrocolic	8 patients	2 patients	16 patients
Totals	9 patients	2 patients	19 patients

Table III. *Influence of the direction of anastomosis upon the incidence of internal hernia in gastrojejunostomy with partial gastrectomy*

	Afferent limb to lesser curvature	*Afferent limb to greater curvature*	*Not stated*
Antecolic	31 patients	5 patients	2 patients
Retrocolic	6 patients	14 patients	4 patients
Totals	37 patients	19 patients	6 patients

tic anastomoses. However, since we do not know the relative proportion in which these types of anastomoses were performed, no valid comparison is possible.

In a description of the direction of the jejunal limb in gastrojejunostomy after partial gastrectomy, an anatomic explanation (that is, whether the afferent limb is attached to the lesser or greater curvature of the gastric pouch) is the most accurate. The results are presented in Table III. Here again, no type of anastomosis is free from the complication of internal hernia.

Length of afferent loop. The length of the afferent loop of jejunum from the ligament of Treitz to the anastomotic line is another variable that might influence the incidence of internal herniation. Unfortunately, this information was lacking in most case reports and, when it was present, the terms "long," "short," and "medium" were used, which made accurate evaluation impossible.

We may conclude that no method of construction of a gastrojejunostomy with or without partial gastrectomy is free of the danger of internal herniation, unless, of course, the retroanastomotic space is actually closed by sutures.

PATHOLOGY OF THE HERNIATED BOWEL

As with hernial rings elsewhere in the abdominal cavity, any mobile structure may be trapped within the confines of the internal hernia which is present after gastrojejunostomy. In an intraperitoneal hernia, the bowel may pass from either right to left or from left to right. As one might expect from the location of the usual gastrojejunostomy which is to the left of the main mass of small-bowel loops, most cases of herniation of the small bowel take place in a right-to-left direction. In such instances, the herniated small bowel comes to lie in the left upper quadrant or left lumbar gutter of the abdomen. In the less common situation in which the small bowel slips through the hernial ring from left to right, it comes to lie in the midabdomen, a location in which the surgeon is accustomed to find the loops of small intestine. Thus, identification of the precise anatomic difficulty may be very difficult for the operator who does not anticipate this complication. Table IV indicates the structures involved and direction of herniation in this type of internal hernia.

In the most frequent type of incarceration, the hernia apparently originates by allowing the efferent limb to slip through the retroanastomotic space. A good portion of the small bowel then follows. In many of the case reports, the entire small bowel had passed through the internal hernial ring except for the last few inches of terminal ileum. Bitman and Stahlgren[3] and Stammers[47] each reported a case in which the greater omentum had passed through the hernial ring. It is not unreasonable to assume that omental herniation may occur more commonly than reported because the signs and symptoms are of less consequence than those of bowel herniation.

Incarceration of the afferent limb of the gastrojejunostomy is of a somewhat more complex anatomic arrangement than was

Table IV. *Direction of herniation and structures involved in 92 cases of retroanastomotic hernia*

	Right to left	*Left to right*	*Not stated*
Gastrojejunostomy without gastrectomy			
Jejunoileum	18	3	9
Afferent limb	0	1	0
Gastrojejunostomy with partial gastrectomy			
Jejunoileum	29	7	2
Afferent limb	21	0	0
Omentum	1	0	1
Totals	69	11	12

Table V. *Position of afferent jejunal limb in retroanastomotic hernias*

	Right to left	*Left to right*
Antecolic anastomosis		
Afferent limb to lesser curvature	19	1
Afferent limb to greater curvature	0	0
Retrocolic anastomosis		
Afferent limb to lesser curvature	1	0
Afferent limb to greater curvature	0	0

described for the more frequent type of internal hernia. If the afferent limb is sufficiently mobile, it may pass through the iatrogenic internal hernial ring in a manner quite similar to that of the rest of the small bowel. Table V, however, shows that of the 21 cases of afferent loop herniations, 19 took place in patients in whom the gastrojejunostomy was antecolic with the afferent limb attached to the lesser curvature of the gastric pouch.

Figs. 3 and 4 help demonstrate the anatomic factors involved in this special variant of retroanastomotic hernia. While the diagram in Fig. 3 is often used to depict the anatomic arrangement in an antecolic, afferent limb to lesser curvature anatomosis, this is not the actual anatomic situation in most cases. In the anastomosis illustrated in Fig. 3, the ligament of Treitz must be situated more medially than is usually found. With the ligament of Treitz situated in its usual position well to the left of the midline, the jejunum and its mesentery must be turned 135° for an anastomosis of the afferent limb to the lesser curvature of the gastric pouch (Fig. 4). The surgeon not only creates an internal hernial ring, but he also places a loop of bowel within its confines. The boundaries of this hernial aperture consist of the efferent limb of the jejunum and its mesentery anteriorly, the ligament of Treitz and gastrojejunostomy superiorly, the transverse colon posteriorly, and the root of the mesentery and mesojejunum inferiorly.

THE CLINICAL MANIFESTATIONS OF THE RETROANASTOMOTIC HERNIA

As with displaced loops of bowel elsewhere, clinical symptoms arise when there is impedance to the flow of bowel content or interference with the blood supply of the bowel. Symptoms may appear anytime from the first postoperative day to 13 years after operation. Cramplike abdominal pain and vomiting, which are the classic symptoms of incarcerated hernias elsewhere, were the most frequent complaints in this group of 92 patients (Table VI). It should be noted that both colic and vomiting were often present, but only the major complaint was listed in Table VI for purposes of tabulation.

Unfortunately, the physical findings in most cases were only minimal, which led to procrastination until the patient was beyond salvage. The "closed loop" has been long recognized as a treacherous diagnostic trap in which the innocuous appearance of the anterior abdominal wall lulls the surgeon into delaying laparotomy. The retroanastomotic hernia is no exception. In addition, after gastrectomy, the surgeon may postulate other causes for the patient's symptoms, such as stomal edema, ninth day syndrome, dumping, psychoneurotic behavior, pancreatitis, and so forth. It should be emphasized that the physical findings are usually not at all dramatic until late in the

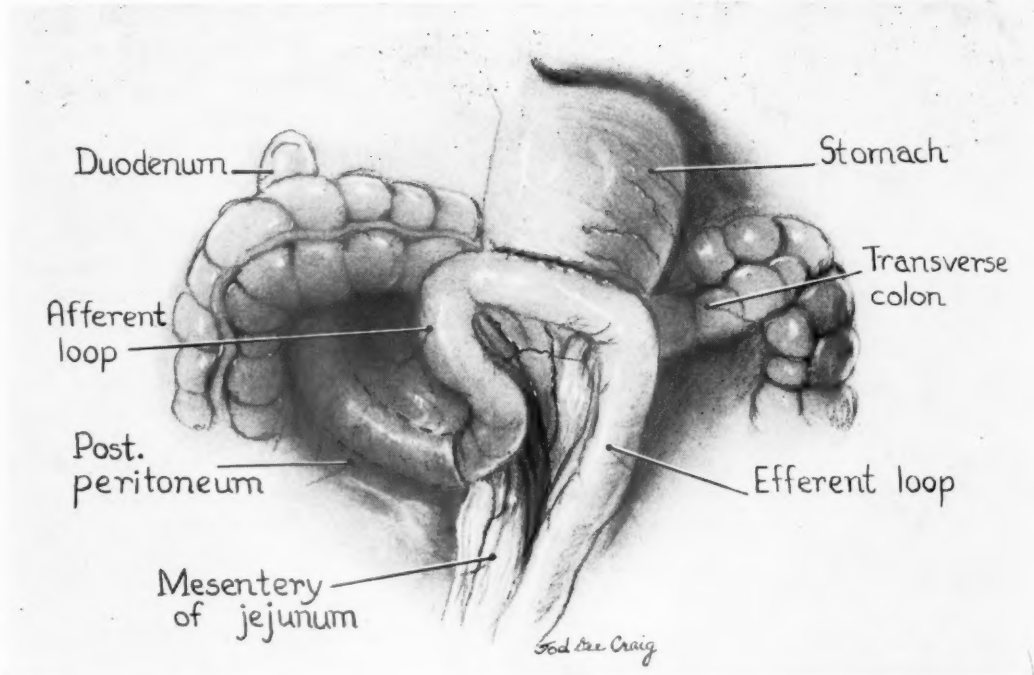

Fig. 3. Antecolic gastrojejunostomy with afferent limb to lesser curvature of gastric pouch.

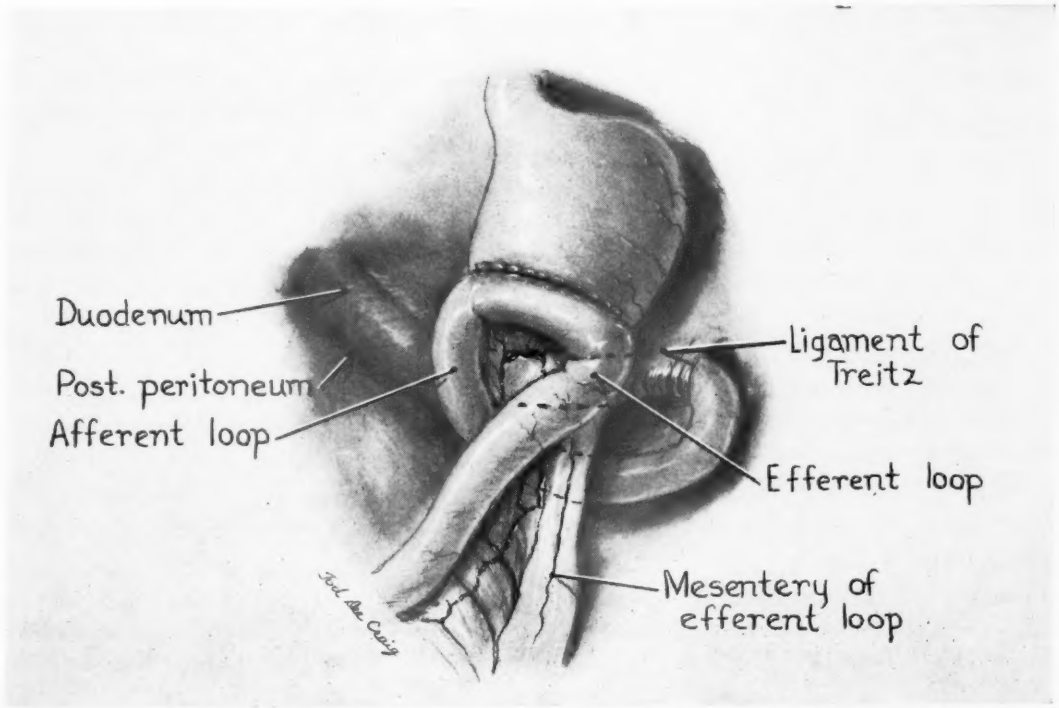

Fig. 4. Antecolic gastrojejunostomy with afferent limb to lesser curvature of gastric pouch in the more usual anatomic position.

Table VI. *Presenting symptom of patients with retroanastomotic hernia*

Symptom	*No. of patients*
Abdominal pain	38
Vomiting	35
Abdominal distention	1
Blood in stools	1
Agitation	1
Sudden collapse	3
Not stated	13
Total	92

Table VII. *Mortality rate of patients with retroanastomotic hernias*

	Lived		*Died*	
	No.	*%*	*No.*	*%*
72 patients treated by operation	49	68	23	32
18 patients treated by nonoperative methods	0	0	18	100
2 patients with information not stated	—	—	—	—
Over-all mortality rate 46%				

course of the complication when strangulation, bowel perforation, and peritonitis supervene. It is undoubtedly the low index of suspicion and resultant delay in diagnosis that have made the fatality rate in this group of patients 46 per cent (Table VII).

TREATMENT

The treatment for this complication is immediate laparotomy, reduction of the hernia, and resection of any gangrenous bowel. At times difficult technical problems may be encountered in the seriously ill patients that require take-down of the gastrojejunostomy and reanastomosis to a different loop of jejunum. In poor-risk patients, when there is incarceration of the afferent limb and viable bowel, an enteroenterostomy may be lifesaving. If the condition of the patient permits, it would behoove the surgeon to close the hernial ring with a few sutures. Bryan[6] reported a case in which a second operation was necessary on the tenth postoperative day to reduce a retroanastomotic hernia after which the internal hernia recurred on the eighteenth postoperative day.

Prevention of this complication by closure of the internal hernial ring is the most satisfactory solution to the problem. Somervell[44] stated in his book on gastric surgery:

> Hernia of the small intestine through the space between the jejunal flexure and the anastomosis is fortunately one of the rarer sequellae of gastrojejunostomy. It can be prevented by a few interrupted sutures of the mesentery to the mesocolon or the band of Treitz. But very few operators do this suturing, and in 5,000 cases in which I have done it only 12 times, I have never seen a case of this hernia.

It is obvious, however, that other surgeons have witnessed this disasterous complication.

It would appear reasonable that closure of the internal hernial ring should be as routine as closing the transverse mesocolon about the gastric pouch in retrocolic gastrojejunostomy or closing the space between a sigmoid colostomy and the lateral peritoneal wall. The exact method by which closure is accomplished will depend upon the particular anatomic arrangement as it is found in each patient and the preference of the operator.[14, 24]

SUMMARY

1. Ninety-two cases of internal hernia after gastrojejunostomy with and without partial gastrectomy were reviewed.

2. The anatomic boundaries of this iatrogenic hernial ring were defined.

3. The propensity of afferent loop herniation in antecolic, afferent loop to lesser curvature anastomoses was described.

4. The mortality rate in patients who underwent laparotomy was 32 per cent. The mortality rate in patients not operated upon was 100 per cent.

5. Closure of the internal hernial ring is believed to be a worthwhile procedure.

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A correlative study of atheromatous embolism in human beings and experimental animals

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Erosion or ulceration of atheromatous plaques of the aorta and its large branches is a commonly encountered pathologic entity. The embolization of the systemic arterial system with material from ulcerated atheromata is mentioned briefly in the older literature,[1] but it remained for Flory,[2] in 1945, to describe the characteristic microscopic appearance of affected vessels and to correctly interpret his findings as representing an embolic phenomenon. To confirm this interpretation, he injected a saline suspension of material from fresh aortic plaques into the ear veins of 2 rabbits. These animals were sacrificed at 24 hours and at 7 days. Lesions resembling those found in human subjects were produced. There was a marked leukocytic response surrounding the arterial lesions at 24 hours, and sequestration of the cholesterol crystals by foreign-body giant cells and scar at 7 days. Both in human beings and in Flory's experimental animals the arterial lesions appeared to result mainly from crystalline cholesterol. Flory further confirmed that embolization was the cause of the arterial changes by correlating the incidence of human subjects affected with the severity of ulcerative atherosclerosis of the aorta.

Since 1945 several papers have been published concerning approximately 90 cases in human beings. In reporting 7 cases, Handler[3] suggested that atheromatous embolization may cause or increase renal hypertension. Probstein and associates[6] reported the cases of 23 patients, 12 of whom showed emboli in the pancreas. Of the 12, 10 had an associated acute pancreatitis. The author concluded, therefore, that atheromatous embolization is an etiologic factor in acute pancreatitis. Meyer[5] and Winter[8] each reported 2 cases of intracerebral artery embolization with small areas of encephalomalacia. Thurlbeck and Castleman[7] described kidney emboli in 15.8 per cent of 38 patients with severe atherosclerosis of the aorta, a figure that rose to 77.3 per cent with the manipulation incident to aortic surgery. Hoye and colleagues[4] reported 1 case of atheromatous embolization of the subcutaneous arteries of gangrenous lower extremities. This is the only instance of peripheral involvement found in a review of the literature.

By virtue of an awareness of and interest in cholesterol embolization, 10 instances were found in a 2-year period at autopsy or in surgically removed tissue. No review of old material was attempted. In 4 of the cases there was involvement of the small arteries of the lower extremities. In addition to tabulation and some consideration of these 10 cases, the results of laboratory experiments will be cited in part. These experiments were undertaken to evaluate the significance of cholesterol embolization and the course of events which follows impaction of this material in small arteries.

CLINICAL STUDY

Pertinent data concerning the 10 clinical cases are recorded in Table I. These cases

Supported in part by United States Public Health Service Grant E-2536.
Received for publication June 23, 1960.

Table I

Case No.	*Age and sex*	*Clinical data*	*Pathologic data*	
			Gross	*Microscopic*
1	63, M	Transmetatarsal amputation of right foot because of nonhealing ulcer	3 cm. ulcer at base of third phalanx	Small artery at base of ulcer occluded with atheromatous embolus (Fig. 9)
2	64, M	Transmetatarsal amputation of left foot because of gangrene of great toe	Gangrene of great toe	Typical atheromatous emboli in 2 small arteries
3	86, M	Ischemia of legs necessitating amputation, death due to a cerebral vascular accident	Complete occlusion of both popliteal arteries, small ulcer over right medial malleolus, and 5 by 6 cm. ulcer over left heel	Several small subcutaneous arteries occluded with atheromatous emboli in both legs, lesions especially prominent at bases of skin ulcers
4	59, M	Splotchy skin rash of both lower extremities, myalgias, and gangrene of left small toe; pedal pulses intact	Skin and muscle biopsy over left calf	Small subcutaneous artery and arteriole in underlying muscle occluded with atheromatous emboli
5	67, M	Bronchogenic carcinoma cause of death	Marked ulcerative atherosclerosis of aorta	Numerous emboli in kidneys, small bowel (Fig. 10)
6	63, M	Died of leakage of suture line 2 months after insertion of aortic graft for arteriosclerotic thoracic aneurysm	Marked atherosclerosis of remaining thoracic aorta and abdominal aorta	Innumerable emboli in the kidneys, adrenal glands, liver, and prostate
7	72, M	Death due to rupture of atherosclerotic aneurysm of abdominal aorta	Marked ulcerative atherosclerosis of aorta, 8 cm. diameter ruptured abdominal aneurysm	Innumerable lesions in kidneys, pancreas, adrenal glands, liver, and gastrointestinal tract
8	74, M	Died of pneumonia complicating uremia, blood pressure 200/100	Marked ulcerative atherosclerosis of aorta, kidneys shrunken	Innumerable lesions in kidneys, several atheromatous emboli in pancreas, adrenals, and gastrointestinal tract
9	66, M	Death due to dissecting aneurysm of aorta with rupture	Rupture of aneurysm into the left pleural cavity, moderate aortic atherosclerosis	Several atheromatous emboli in small renal and adrenal arteries
10	75, F	Myocardial infarction with death due to a cerebral vascular accident	Myocardial infarction, mural thrombosis, and embolization of middle cerebral artery; moderate aortic atherosclerosis	A few atheromatous emboli in small arteries of kidneys, pancreas, and adrenal glands

were encountered in the period from December, 1957, to December, 1959. Six of the cases were discovered at autopsy examination, and the other 4 by examination of surgical specimens.

Case 4 of our series clearly demonstrates the occurrence of peripheral arterial involvement.

Case 4. J. S., a 59-year-old white male barber, was admitted to Vanderbilt University Hospital for the first time on Nov. 3, 1959, complaining of "painful feet" of 7 to 10 days' duration.

In July, 1959, the patient had had a "heart attack" and was treated with anticoagulants. Some 3 weeks later he noted pain in his left small toe. In September, 1959, he had another "heart attack" and during his 6 weeks' hospitalization developed progressive gangrene of the left small toe.

Three weeks before admission he had noted the onset of an erythematous rash over his feet, legs, and buttocks which cleared intermittently. General myalgias were noted with fairly severe pain in the toes and mild pain in the legs and arms.

Physical examination showed a thin white male who complained of pain in his feet on ambulation. Pertinent findings were limited to the skin and lower extremities. The pedal pulses were "full and bounding" bilaterally. The feet were warmer than the legs, but the toes were cold with a bluish discoloration. The left fifth toe was gangrenous. An erythematous macular and sometimes confluent rash was noted over the abdomen, buttocks, legs, and feet.

Laboratory data. Results of urinalysis showed 2 to 3 plus protein. There were 30 to 40 red blood cells per high power field and 2 to 5 white blood cells per high power field. The hemogram was essentially normal. The cholesterol was 420, stool was 1 plus for occult blood, and the L. E. preparation was negative.

Special procedures. A gastrointestinal series showed a chronic duodenal ulcer. An electrocardiogram revealed anterior myocardial infarction of indeterminate age.

Hospital course. The gangrene of the patient's left small toe progressed relentlessly. Because of suspected arteritis, steroid therapy was instituted. A skin and muscle biopsy of the right posterior calf was obtained. The patient was discharged to the care of his private physician.

Microscopic examination of skin and muscle. The squamous epithelium was normal in appearance. One medium-sized artery in the underlying fat was occluded by a cholesterol embolus (Fig. 1), as was a smaller artery in the section of muscle (Fig. 2). There was underlying chronic inflammatory infiltrate adjacent to an occluded artery in the muscle. The muscle fibers were unremarkable. All the other arteries appeared normal.

Comment. The cholesterol embolization was believed adequate to explain the rash, myalgia, and gangrene of the left small toe.

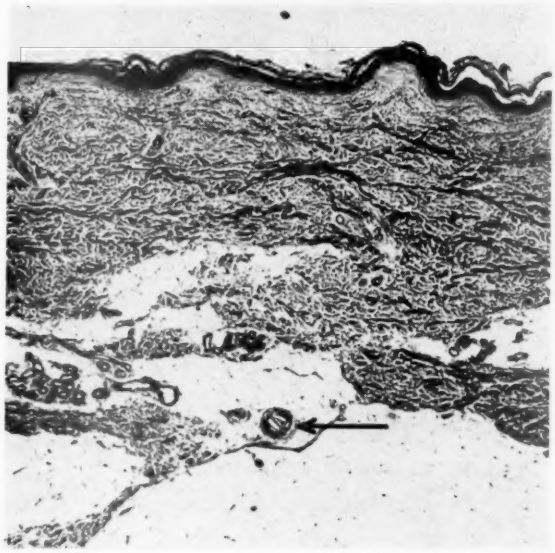

Fig. 1. Case 4. Photomicrograph of the skin biopsy specimen with the small vessel in the subcutaneous fat exhibiting the effects of cholesterol embolism (arrow). (Hematoxylin and eosin; ×80; reduced ⅓.)

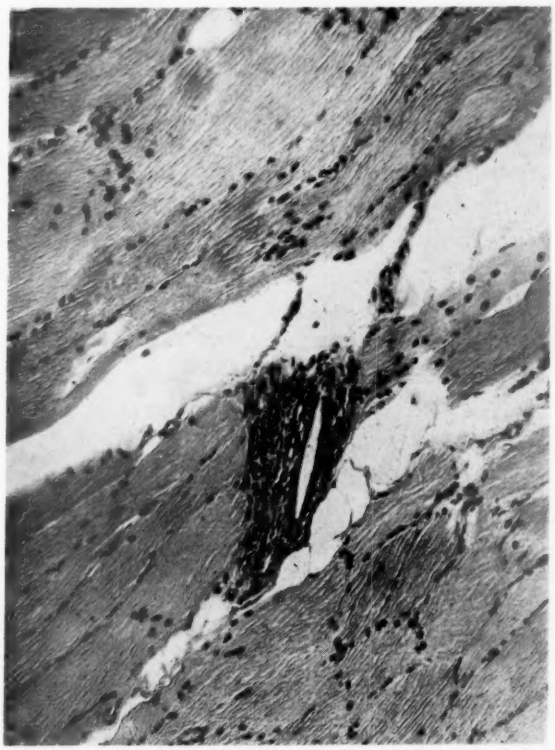

Fig. 2. Case 4. Photomicrograph of the muscle biopsy specimen. This shows a striking example of the inflammatory process which occurs after cholesterol crystal embolization. (Hematoxylin and eosin; ×235; reduced ⅓.)

Though the evidence of previous myocardial infarction suggests the possibility of mural thrombosis with embolization of small fragments, such emboli were not found. The appearance of vessels with impacted cholesterol is entirely distinctive and the anisotropic character of the cholesterol is a final identifying feature.

In order to study cholesterol embolism in a controlled situation, animal experiments were undertaken.

EXPERIMENTS

Sixteen rabbits which weighed approximately 5 pounds, and 9 mongrel dogs were used in the experiments.

It is impossible to suspend cholesterol crystals uniformly in saline solution but this material may be satisfactorily suspended in serum. Stock suspensions of 10 mg. cholesterol* per milliliter of rabbit and dog serum were prepared and stored at 5° C.

Rabbits.

Injection. Varying amounts (5 to 50 mg.) of the cholesterol suspensions were injected into the marginal ear vein of rabbits by means of tuberculin syringes and 18 gauge needles.

Sacrifice. The rabbits were sacrificed at varying intervals (Table II) by means of intravenous barbiturates. The lungs were fixed in formalin.

Microscopic study. Routine hematoxylin and eosin stained sections of the formalin-fixed tissues were made. Frozen sections were prepared, and polarized light was used to identify the anisotropic cholesterol crystals.

Results (Table II). There were no gross lesions. In all the animals cholesterol clefts† could be easily identified microscopically in many of the small and medium-sized pulmonary arteries, and there was an acute inflammatory response with numerous leukocytes and eosinophils. This reaction was evident within 1 day after injection (Fig. 3). In some instances a fibrin mesh was identifiable surrounding the cholesterol. By 3 days (Fig. 4) there was a panarteritis with a remarkable number of eosinophils present. The intima was quite hyperplastic, numerous leukocytes surrounded the adventitia, and foreign-body giant cells were present. At 6 days the acute process had almost subsided and foreign-body giant cells surrounding the cholesterol particles were conspicuous. By 12 days (Fig. 5) there was intimal fibrosis and sequestration of the crystals by foreign-body giant cells. Many of the arteries involved were completely occluded by fibrosis. There were no discernible changes in the number or appearance of the lesions at 67 days (Fig. 6). The cholesterol crystals seemingly acted as permanent foreign bodies, as partial or complete occlusion of the affected vessels (Fig. 7) was demonstrated 160 days after injection when the experiment was terminated.

Dogs.

Injection. The left femoral artery was isolated through a skin incision. The cholesterol suspension was injected intra-arterially just

Table II

Rabbit No.	*No. of days injection to sacrifice*	*Lesions*	
		Gross	*Microscopic*
1	1	Patchy atelectasis	Acute periarteritis
2	3	None	Subsiding periarteritis
3	6	None	Sequestration of crystals with giant cells
4	12	None	Same
5	24	None	Same
6	24	None	Same
7	25	None	Same
8	64	None	Same
9	67	None	Same
10	67	None	Same
11	80	None	Same
12	80	None	Same
13	128	None	Same
14	128	None	Same
15	128	None	Same
16	160	None	Same

There is a subjective correlation of the number of embolic lesions present to the amount of cholesterol injected. There was no apparent decrease in the number of lesions with time.

*Cholesterol crystals, U.S.P.

†Routine preparation of hematoxylin and eosin sections dissolved the cholesterol crystals.

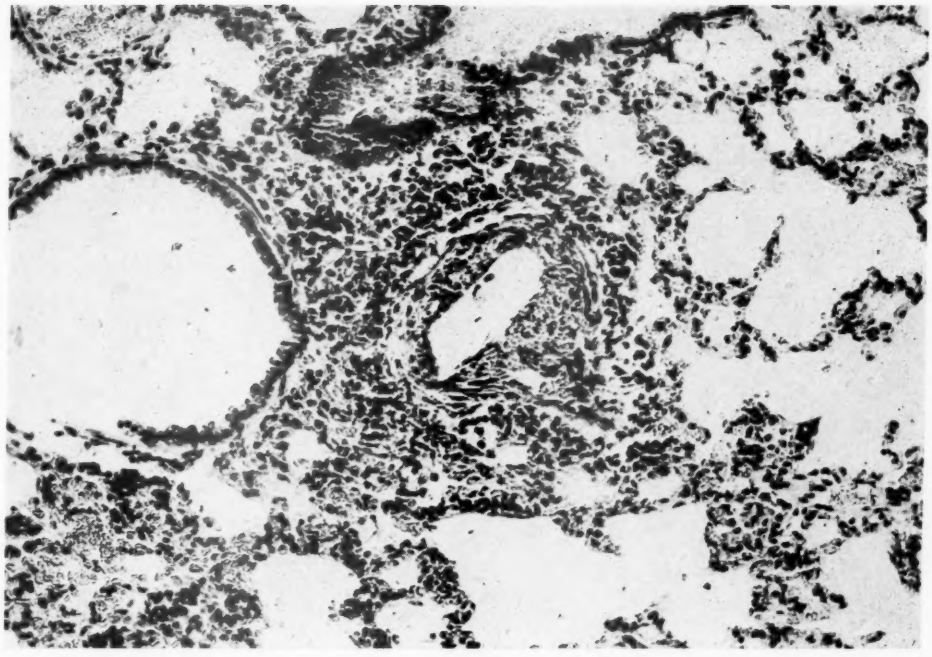

Fig. 3. Photomicrograph of rabbit's lung 1 day after injection of cholesterol crystals. Note the intense acute inflammatory response. (Hematoxylin and eosin; ×200; reduced 2/7.)

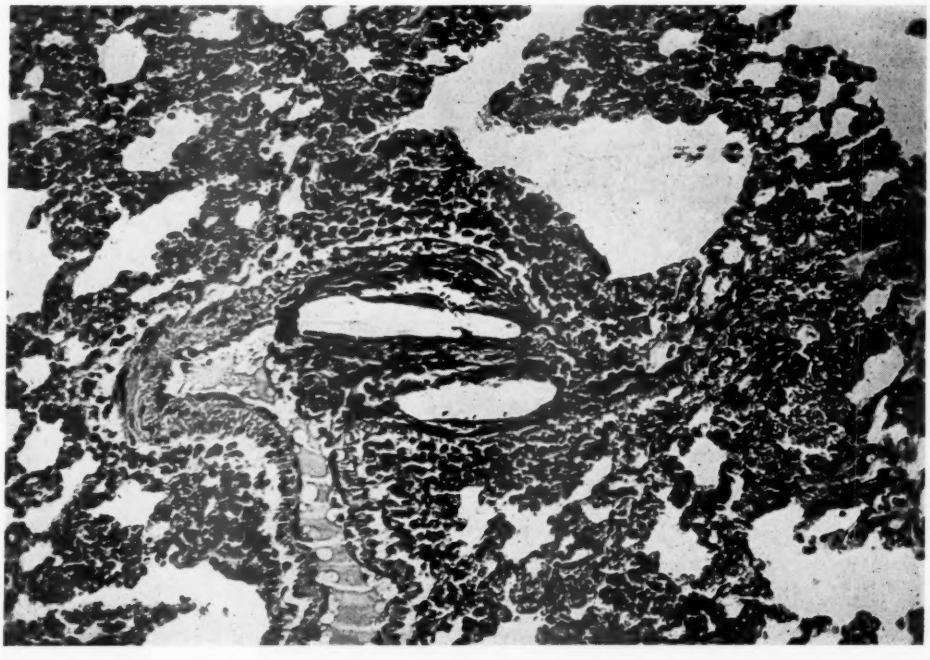

Fig. 4. Rabbit 2. Photomicrograph of rabbit's lung 3 days after injection of cholesterol crystals. The acute inflammatory response has begun to subside, and foreign-body giant cells are forming. (Hematoxylin and eosin; ×200; reduced 2/7.)

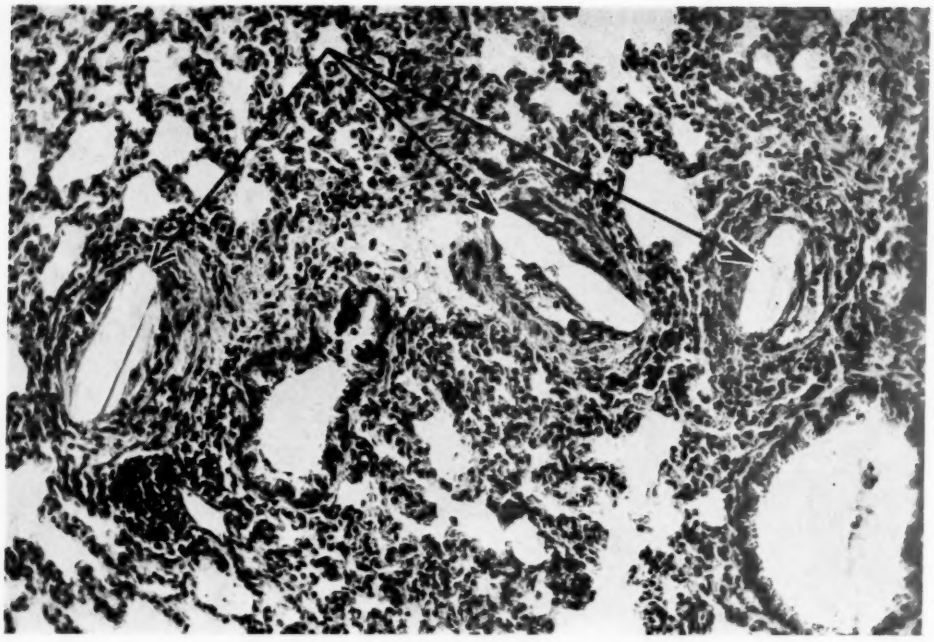

Fig. 5. Rabbit 4. Photomicrograph of rabbit's lung 12 days after injection of cholesterol crystals. The crystals have been sequestrated by foreign-body giant cells. Note the absence of acute inflammatory cells. (Hematoxylin and eosin; ×200; reduced 2/3.)

distal to the inguinal ligament with a tuberculin syringe and an 18 gauge needle. The right femoral artery was ligated in many of the dogs as a control. It was difficult to prevent thrombosis at the injection site.

Sacrifice. The dogs were sacrificed by intracardiac injection of ether. The femoral arteries were inspected. The legs were disarticulated and fixed in formalin.

Microscopic study. Routine hematoxylin and eosin stained sections of the formalin-fixed tissues were prepared.

Results (Table III). We were able to produce gangrenous changes in the hind feet of several dogs (Fig. 8), but only in cases in which there was associated thrombosis of the femoral artery. It is well known that, in the dog, mere ligation of the femoral artery above produces no functional or anatomic changes. Hematoxylin and eosin stained sections revealed several arteries occluded by the cholesterol crystals. These were indistinguishable from the human lesions. As in the rabbit, the crystals persisted as foreign bodies. Three dogs followed for 30 days had persistence of cholesterol in the arterial lesions.

Discussion. It is believed that these studies have established the thesis that cholesterol embolization may play an important role in some cases of peripheral gangrene by virtue of impaction in the small arteries. The demonstrated persistence of arterial occlusion in the experimental animal for periods of as long as 160 days substantiates the opinion that, in human beings, episodic occurrence of cholesterol embolization can sufficiently compromise the circulation to the extent that ischemic necrosis may occur. No definite evidence of re-establishment of the arterial lumen has been noted once the occlusion has occurred, and it is likely that the small artery so involved is lost to the circulation. The role of cholesterol embolism in some cases of pancreatic necrosis, in renal arterial occlusive disease (Fig. 10), and, as pointed out in the present studies, in the pathogenesis of ischemic necrosis in the extremities (Fig. 9) is better understood in the light of the experi-

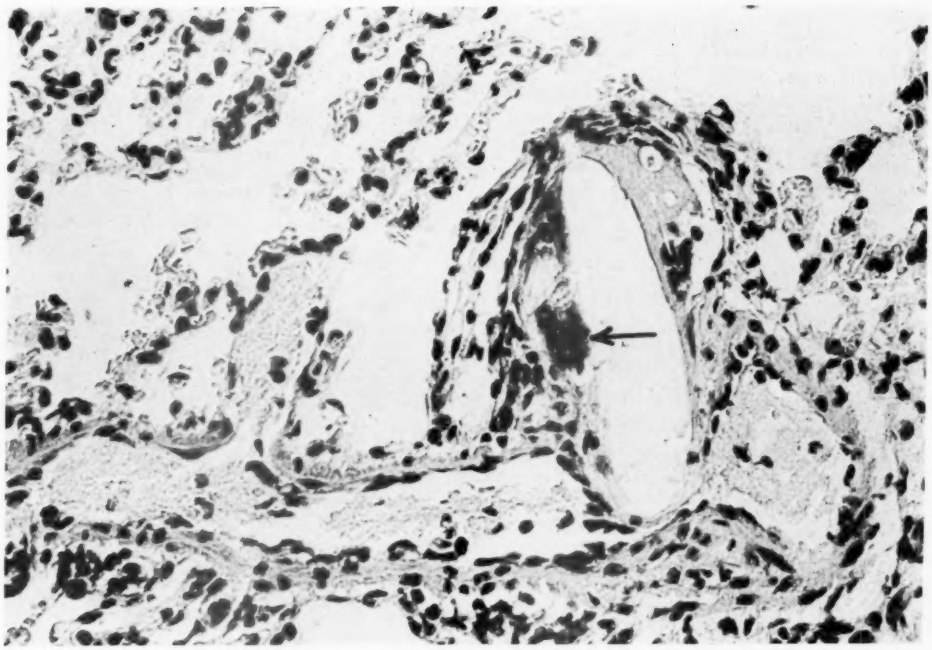

Fig. 6. Rabbit 9. Photomicrograph of rabbit's lung 67 days after injection of cholesterol crystals. Note the large foreign-body giant cell (arrow). (Hematoxylin and eosin; ×280; reduced 2/7.)

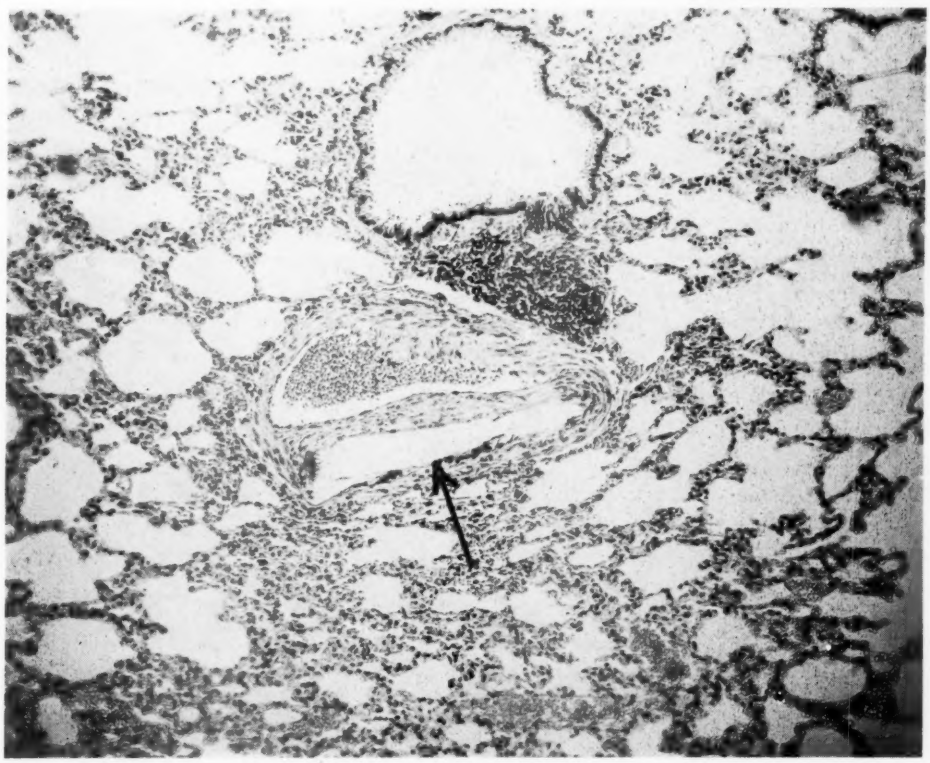

Fig. 7. Rabbit 16. Photomicrograph of rabbit's lung 160 days after injection of cholesterol crystals. The crystal persists intravascularly as a permanent foreign body (arrow). Note the similarity of this lesion to the ones in Fig. 5. (Hematoxylin and eosin; ×200; reduced 2/5.)

Table III

Dog No.	*Amount of cholesterol injected (mg.)**	*No. of days injection to sacrifice*	*Pathologic findings*	
			Gross	*Microscopic*
1	80	2	Gangrene of foot, thrombosis of femoral artery	Cholesterol emboli in many small arteries and arterioles
2	50	2	Gangrene of foot, thrombosis of femoral artery	Same
3	25	2	Gangrene of foot, thrombosis of femoral artery	Same
4	50	10	Gangrene of toes, developed slowly; thrombosis of femoral artery	Same
5	35	12	Gangrene of toes, developed slowly; thrombosis of femoral artery	Cholesterol crystals surrounded by giant cells in many small arteries and arterioles
6	50	22	Leg normal, femoral artery patent	Same
7	20	30	Leg normal, femoral artery patent	Same
8	20	30	Leg normal, femoral artery patent	Same
9	20	30	Gangrene of foot, thrombosis of femoral artery	Same

*In all the dogs the left femoral artery was used for injection of cholesterol.

mental demonstration of permanent closure of small end arteries by this mechanism.

It is doubtful that this mechanism of vascular occlusion is entirely responsible for cases of ischemic necrosis encountered clinically, even though demonstrably present. It seems more probable that in most cases embolism with cholesterol would represent a contributing or additive factor in ischemic necrosis, with the vascular supply already seriously compromised by atherosclerosis or other occlusive lesions. An experimental counterpart is seen in the case of the femoral artery injection in dogs. Neither arterial thrombosis alone nor rather massive cholesterol embolism by itself would produce peripheral gangrene in the dog's foot, whereas if the two were simultaneously operative, ischemic necrosis would ensue.

The persistence of cholesterol and its role as a foreign body is of interest. This fact and its occurrence in massive amounts in sites of old hemorrhage would suggest that enzymatic breakdown of cholesterol is not possible in these circumstances even though synthesis of this material has been demonstrated to occur in a variety of tissues.

SUMMARY

1. Ten cases of atheromatous embolization are presented. Lower extremity involvement was demonstrated in 4.

Fig. 8. Dog 4. Photograph of dog's feet 10 days after injection of cholesterol (50 mg.). The left foot is gangrenous.

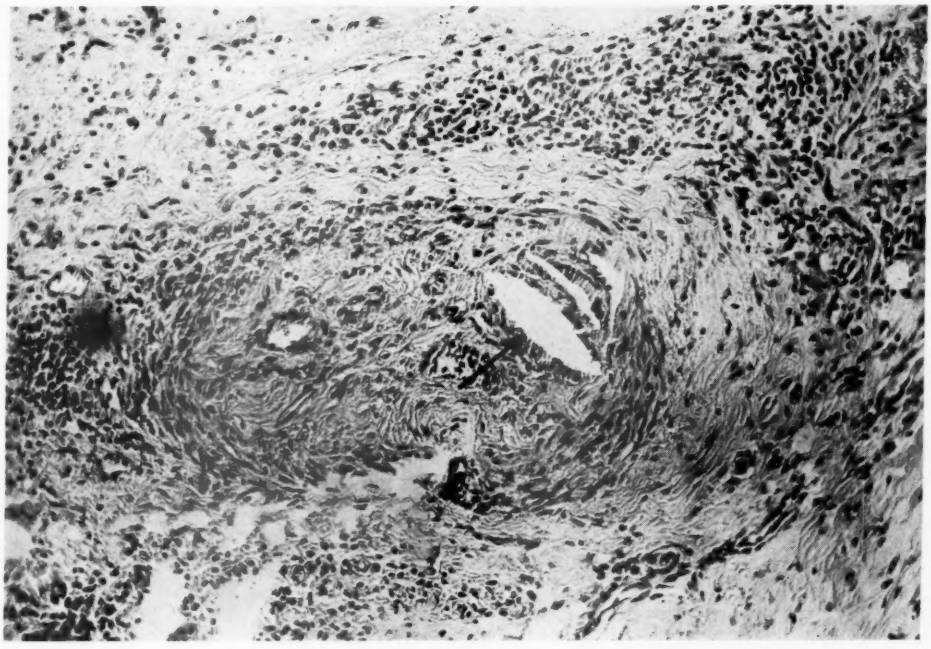

Fig. 9. Case 1. Photomicrograph of a section taken from a "trophic ulcer" at the base of the third phalanx of the right foot. This is a typical lesion, with cholesterol clefts (arrow), intimal fibrosis, and occlusion. The surrounding cellular response has resulted from proximity to the ulcer. (Hematoxylin and eosin; ×245; reduced 2/7.)

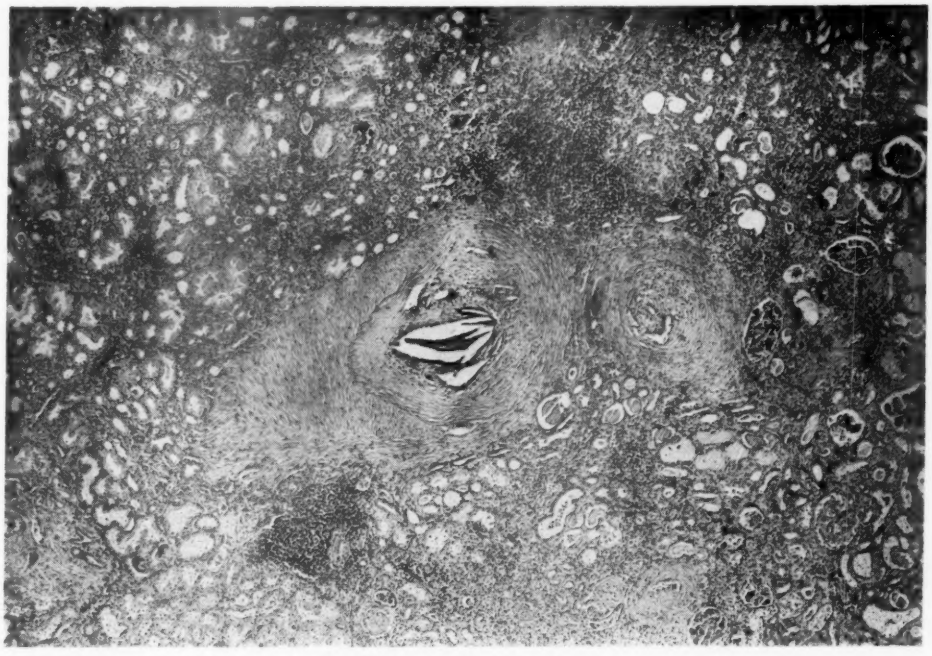

Fig. 10. Case 5. Photomicrograph of kidney. The interlobular artery is completely occluded with a typical atheromatous embolus. The cholesterol clefts are quite large in this instance. (Hematoxylin and eosin; ×80; reduced 2/7.)

2. Experimental work has demonstrated the persistence of intravascular cholesterol crystals for long periods of time.

3. The role of atheromatous embolization producing gangrenous changes in the lower extremity is presented.

We wish to thank Dr. W. Andrew Dale for the use of Case 3 and the suggestions which he has made in this investigation.

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Superior vena cava to pulmonary artery shunt for tricuspid atresia in an infant

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It has been demonstrated by the animal work of Glenn[5, 6] and Robicsek,[9] and more recently by a small number of clinical cases reported by Glenn,[4] Sanger,[10] Bakulev,[1] and Gasul[3] and their associates that 35 to 45 per cent of the total cardiac venous return can be diverted directly to the pulmonary arteries without passing through the right side of the heart. This not only improves systemic arterial oxygen saturation, but also diminishes the amount of blood which must flow through the right side of the heart and, in a patient with tricuspid atresia, decreases the amount of blood which must flow through the atrial septal defect into the left atrium and ventricle. Anastomosis between the superior vena cava and distal right pulmonary artery has been reported in complete transposition with pulmonic stenosis by Glenn,[4] Sanger,[10] and Rasmussen[8] in patients aged 7 years 11 years, and 14 months, respectively. Gasul and associates[3] reported the same procedure in 3 patients (ages 4, 8, and 14 years) with Ebstein's anomaly of the tricuspid valve with success in 2. Bakulev and Kolesnikov[1] presented 41 cases of tetralogy of Fallot in which this procedure was performed with a 36 per cent mortality rate. There is a total of 47 reported cases of circulatory bypass of the right side of the heart.

Although all of the authors mentioned have suggested that tricuspid atresia might be benefited by this operation, such a case has not been reported. Also, as far as we know, ours is the youngest patient to have been subjected to bypass of the right side of the heart with success. This is interesting in view of the small size of the vessels encountered and the comment by Nuland, Glenn, and Guilfoil,[6] "It is doubtful if the anastomosis will remain patent if it is small. It may therefore not be possible to apply this technique successfully in the infant with small vessels."

This work was performed with the assistance of a grant from The Alabama Heart Association and United States Public Health Grant H-1987C5.
Received for publication June 9, 1960.

CASE REPORT

E. M. S., a 14-week-old white male, was first seen at the age of 6 weeks with a history of cyanosis since birth and liver enlargement discovered at 6 weeks of age. He was an obese infant with moderate cyanosis and an arterial saturation of 65 per cent while breathing air. A systolic murmur was present to the left of the sternum in the third intercostal space and there was marked subcostal retraction present with a respiratory rate of 40 to 60 per minute. The liver was felt 3 cm. below the right costal margin. The electrocardiograph revealed left ventricular hypertrophy and left axis deviation. A roentgenogram showed a small heart with a straight left border and the vascularity of the lung fields was slightly decreased. The diagnosis of tricuspid atresia was made and it was elected to watch the infant.

Four weeks later, the child was again seen. At this time he had begun to develop severe dyspnea and spells of anoxia. Marked

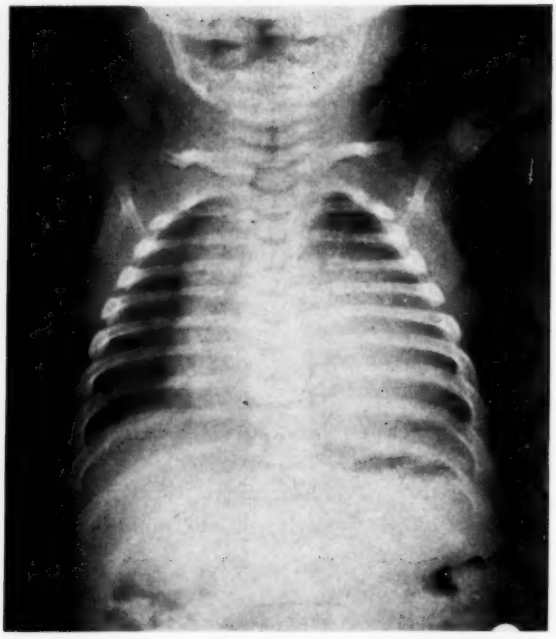

Fig. 1. Preoperative chest roentgenogram which shows patient with tricuspid atresia with huge heart in failure.

Fig. 2. Immediate postoperative chest roentgenogram shows rapid decrease in heart size after shunt.

sweating was present at all times and subcostal retraction was greatly increased.

On physical examination the liver was found to be down to the umbilicus and a roentgenogram showed the heart to fill the left side of the chest (Fig. 1). Digitalis was administered in the form of Lanoxin and the child responded well to this. Two days later the liver was again felt at 3 cm. below the costal margin and the heart had decreased markedly in size. Cardiac catheterization was undertaken and cineangiocardiograms revealed tricuspid atresia with an atrial and ventricular septal defect and pulmonic stenosis. The condition was classified as Edwards' type Ib.[2]

Since the child had improved, it was elected to continue watching him. Three weeks later, he again began having spells of severe restlessness and paroxysmal dyspnea, during which time he would lose consciousness momentarily. It was decided that operation could no longer be deferred. At this time the child was 14 weeks old.

At operation on March 30, 1960, through a right fourth intercostal incision the right pulmonary artery was detached from the main pulmonary artery and the distal end sutured end-to-side to a longitudinal incision in the superior vena cava at a convenient spot below the azygous vein. A continuous everting No. 5-0 silk suture was used posteriorly while the anterior row was of interrupted sutures to allow growth between stitches. The vena cava was partially occluded for 14 minutes while the anastomosis was accomplished. During this period the face was dusky but there was no serious venous engorgement. Color returned to normal after the clamps were released. The right pulmonary artery was small, one-third smaller than the vena cava at this level. After completion of the anastomosis the superior vena cava central to this vein-artery connection was ligated, which diverted all superior caval blood through the right lung. The azygous vein was also ligated. After the chest incision had been closed a tube gastrostomy was performed to prevent gastric distention or regurgitation.

The first postoperative film showed a marked decrease in heart size and lung fields of normal vascularity with remarkably few postoperative changes (Fig. 2). The liver was markedly diminished in size during the whole first 2 days. The first 24 hours were quite smooth, but at the end of the second day, respiratory distress developed, and roentgenogram showed complete atelectasis of the left lung. A tracheotomy was performed and repeated trachial and bronchial suction was instituted, which resulted in almost immediate complete expansion of the lung. The child's color, which had become a little worse in the period of difficulty, began to improve and during the second week of his postoperative course the color was quite excellent. During this time, arterial oxygen saturation was between 80 and 85 per cent while the patient was breathing air. There have been no further spells of dyspnea or restlessness, although sweating is still noticed. It is of interest that the child tolerates the prone position as well as a semierect position and, in fact, can be held upside down without difficulty. When he cries, there is quite an increase in cyanosis, but this clears immediately when he stops.

That the condition of this 14-week-old child with well-documented tricuspid atresia could be improved by right pulmonary artery—superior vena cava anastomosis is encouraging. At least it demonstrates that a small anastomosis in the low-pressure venous system can remain patent. The rapid decrease in heart size and complete disappearance of liver congestion give dramatic evidence of reduction of the flow through the right side of the heart and through the atrial septal defect, while the improvement in oxygen saturation is indicative of a satisfactory pulmonary flow. Such improvements in heart size, right atrial congestion, and cyanosis do not usually follow the construction of a Blalock or Potts shunt to the pulmonary artery. If subsequent experience with the vena cava–pulmonary artery shunt is as favorable as in this case, this would seem to be the operation of choice for tricuspid atresia.

In all cases of bypass of the right side of the heart previously reported except the single case of Glenn the patients were operated on with an end-to-end anastomosis between the superior cava and distal right pulmonary artery. This technique may have 2 serious disadvantages. First, serious symptoms of cerebral congestion may develop from temporary but complete occlusion of the superior cava. Bakulev and Kolesnikov[1] state that most of their patients leave the operating room with marked cyanosis and edema of the face, and that the face and upper half of the body are covered by petechiae in most cases. They also comment that electroencephalographic monitoring shows severe cerebral depression during caval occlusion. Using the end-to-side method developed by Glenn and colleagues[4] one avoids this hazard by partially occluding the vena cava during the anastomosis. The superior vena cava is occluded completely by ligature only after there is free flow into the pulmonary artery.

The second occasional disadvantage of direct end-to-end vena cava–pulmonary artery anastomosis is discrepancy in size. The pulmonary artery is often considerably smaller than the superior vena cava and end-to-end suture may be difficult to accomplish without folds and uneven surfaces, in which case thrombosis is almost certain. With the end-to-side technique a neat and accurate suture anastomosis can be constructed to a proper-sized longitudinal incision in the vena cava. Therefore, the end-to-side technique of Glenn would seem to offer definite advantages.

SUMMARY

A shunt between the superior vena cava and the distal right pulmonary artery was successfully accomplished in a 14-week-old infant with well-documented tricuspid atresia. This effectively diminished the right atrium, decongested the liver, and improved oxygen saturation. As far as we know, ours is the youngest patient and also the first patient with tricuspid atresia to undergo bypass of the right side of the heart successfully.

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The effect of total body perfusion on carotid blood flow

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Cerebral depression frequently follows periods of extracorporeal cardiopulmonary bypass in animals and occasionally serious central nervous system changes are observed in patients after perfusion. In some instances, these episodes of cerebral dysfunction are probably due to particulate or air emboli. But in other cases, no explanation is readily apparent unless cerebral blood flow was inadequate during perfusion. For a more detailed understanding of the effect of perfusion upon cerebral blood flow, carotid artery flow was measured in dogs before, during, and after perfusion. Flow measurements and pressure determinations made possible an analysis of cerebral vascular resistance changes.

METHODS

Mongrel dogs were anesthetized with Surital. Intubation was carried out and respiration was maintained by intermittent positive pressure with ambient air. The chest was opened either through the right fifth intercostal space or by splitting the sternum in the midline. Catheters were inserted in the vena cava and a cannula was placed in the right femoral artery. Catheters and cannulae were connected to a heart-lung machine which consisted of roller pumps and a rotating disc Kay-Cross oxygenator. The dogs were perfused at the rate of 100 ml. per kilogram per minute for an average of 60 minutes.

In 6 animals, a rotameter[8] was inserted into the right common carotid artery. In 4 additional animals, in which the sternum had been split, the rotameter was inserted into the brachiocephalic artery. In these 4 animals, the right subclavian and both vertebral arteries were ligated. Thus the rotameter in the brachiocephalic artery monitored all the blood flow going into both carotid arteries. These 4 dogs are referred to as the total carotid artery flow group. The rotameter was calibrated at the end of each experiment with blood from the animal.

Carotid pressure and flow were measured before perfusion, during perfusion, and after extracorporeal circulation had been discontinued. Carotid vascular resistance at similar pressure levels was calculated for these 3 periods by the equation $R = P/F \times 100$. P represents mean carotid artery pressure and F represents flow in milliliters per minute.

One hundred per cent oxygen was passed through the oxygenator except for a 10-minute period when a 3 per cent carbon dioxide and 97 per cent oxygen mixture was used to oxygenate the blood. In this way, carbon dioxide tension was raised to study its effect upon carotid blood flow during perfusion.

During each experiment superior vena caval pressure, systemic pressure, and elec-

Supported by a grant from the Cleveland Area Heart Society.
Received for publication June 9, 1960.
*Work was carried out in partial fulfillment of the requirements for the M. D. degree at Western Reserve University.

Table I

Experiment No.		*Flow (ml./min.)*	*Pressure (mm. Hg)*	*Arterial pH*	*R = P/F*	*% change in R*	
147	Control	32	60	7.31	1.9		
	Perfusion	70	100	7.10	1.4	−26	
	After perfusion	30	58	—	1.9		0
148	Control	48	80	7.34	1.7		
	Perfusion	60	82	7.29	1.37	−17	
	After perfusion	50	82	7.23	1.6		−6
149	Control	50	104	7.28	2.08		
	Perfusion	88	90	7.09	1.04	−50	
	After perfusion	102	80	7.16	0.78		−62
150	Control	58	62	7.29	1.07		
	Perfusion	68	58	6.99	0.85	−20	
	After perfusion	108	68	—	1.63		−41
158	Control	48	84	7.32	1.75		
	Perfusion	70	72	7.11	0.97	−45	
	After perfusion	65	42	—	0.65		−63
161	Control	25	85	7.19	3.4		
	Perfusion	46	82	7.05	1.8	−47	
	After perfusion	96	85	—	0.9		−74
162	Control	52	89	7.29	1.71		
	Perfusion	70	92	7.12	1.31	−23	
	After perfusion	54	96	—	1.78		+6
163	Control	118	92	7.37	0.77		
	Perfusion	192	115	7.20	0.60	−22	
	After perfusion	190	112	—	0.59		−23
164	Control	34	50	7.37	1.47		
	Perfusion	132	77	7.11	0.58	−60	
	After perfusion	76	40	—	0.53		−64
167	Control	92	98	7.36	1.06		
	Perfusion	152	110	7.22	0.72	−32	
	After perfusion	142	104	—	0.73		−31

trocardiogram were measured and recorded at appropriate intervals by means of a photographic electronic recorder.

Arterial and venous samples were drawn at the beginning and end of perfusion and analyzed for pH, carbon dioxide, oxygen, hemolysis, and hematocrit. Samples were also taken and measured for pH, carbon dioxide, and oxygen before and at the end of a 10-minute period during which carbon dioxide was added to the oxygenator. Carbon dioxide tension was calculated by means of the normogram of Van Slyke and Sendroy.[9]

Carotid pressure and flow during perfusion. In Table I, carotid flow during perfusion is compared with control flows at similar pressures. In all experiments, the carotid flow for a given pressure was greater during perfusion than during the control period. Thus, perfusion markedly reduces carotid vascular resistance. Similar information is shown graphically in Fig. 1. In this illustration, the open bars represent the per cent fall in resistance during perfusion when the control resistance value represents 100 per cent. As can be seen, the resistance falls as much as 50 to 60 per cent during bypass.

Carotid pressure and flow after perfusion. Table I also lists the carotid flow rates after perfusion at pressures similar to control levels. In 7 animals, the flow rate was sig-

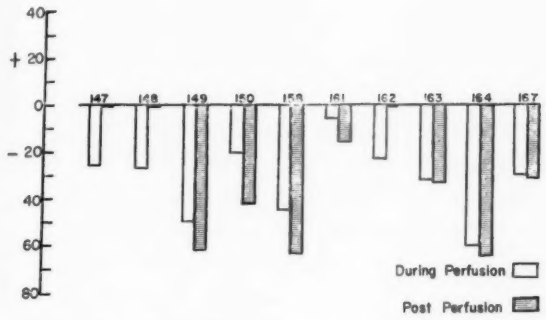

Fig. 1. Per cent change in carotid vascular resistance during and after total body perfusion.

nificantly greater than control levels. As is shown in Fig. 1, the carotid vascular resistance in these animals was markedly reduced (solid bars). However, in 3 experiments (Nos. 147, 148, and 162), the flow rate and pressure relationships were the same after perfusion as during the control period. Therefore, in these dogs, carotid vascular resistance returned to the preperfusion level after bypass.

Original records (Fig. 2) taken from experiment No. 167 (total carotid flow) clearly illustrate the changes in cerebral vascular resistance which resulted from perfusion. Fig. 2, *A*, shows control values for pressure, carotid flow, and superior vena cava pressure. Fig. 2, *B*, shows the changes in these values during cardiopulmonary bypass, and Fig. 2, *C*, depicts the findings after perfusion. It should be noted that there was a marked increase in cerebral flow rate during and after perfusion even though the carotid artery pressure was essentially the same as that during the control period.

Effect of carbon dioxide tension upon carotid blood flow. The addition of 3 per cent carbon dioxide to the oxygenator for a period of 10 minutes resulted in a significant rise in carbon dioxide tension. However, as can be seen in Table II, the change in carotid vascular resistance was variable. In 5 animals the resistance increased, in 4 it decreased, and in 1 there was no change. These resistance changes were primarily due to changes in flow. In the instances in which flow decreased, resistance rose, and when flow increased, resistance fell. Carotid artery pressure remained about the same throughout carbon dioxide administration.

Effect of increasing superior vena caval pressure upon carotid blood flow. In this part of the experiment, there was a significant difference between the animals in which flow through both carotid arteries was measured (Nos. 161, 163, 164, and 167) and those in which only one carotid artery was monitored with the rotameter. In the latter group of dogs, a decrease in flow was seen only after superior vena

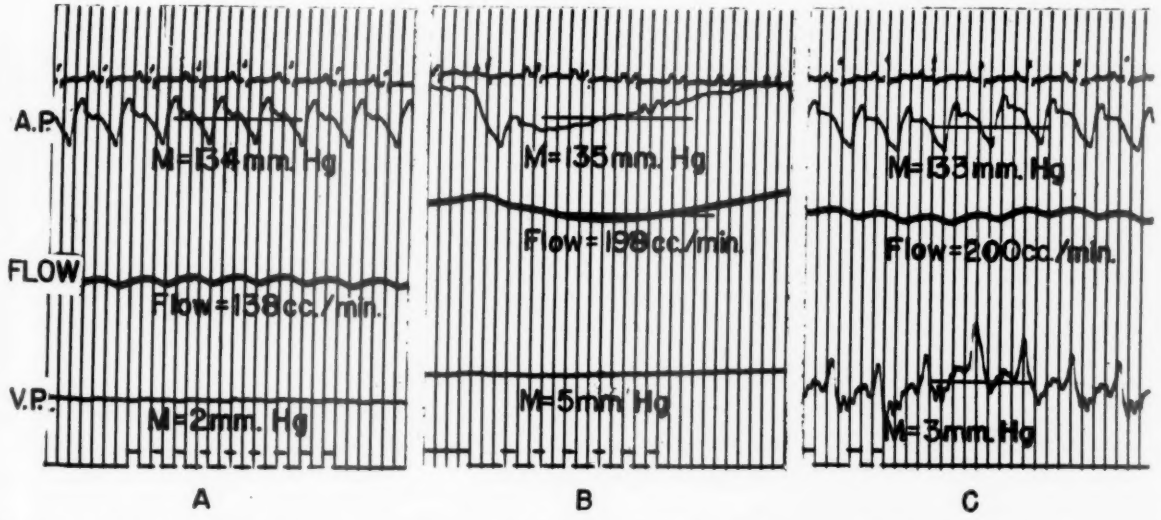

Fig. 2. Original records taken from experiment No. 167 which shows changes in carotid artery pressure, carotid blood flow, and central venous pressure, *A*, before, *B*, during, and *C*, after total body perfusion

Table II. *Effect of increasing carbon dioxide tension upon carotid vasculature resistance*

Experiment No.	*pCO_2 (mm. Hg)*		*% change in carotid vascular resistance*
	Initial	*Final*	
147	33	47	−10
148	28	44	0
149	37	51	+ 3
150	33	51	+12
158	29	45	−50
161	30	50	+30
163	25	36	−29
164	21	31	−20
166	30	59	+ 6
167	25	45	+10

caval pressure exceeded 20 mm. Hg. In contrast, as shown in Fig. 3, in the animals in which total carotid flow was measured, vena cava pressures above 10 mm. Hg resulted in a significant fall in carotid blood flow.

DISCUSSION

Carotid blood flow measurements in these experiments included not only the cerebral flow, but also blood entering the external carotid bed. Nevertheless, these observations probably reflect relative changes in the cerebral vascular bed, for Rosomoff and Holaday,[7] while studying cerebral blood flow with hypothermia, concluded that carotid blood flow measurements even with other circulatory beds included (as in our experiments) gave valid results when compared with results obtained when cerebral blood flow alone is measured. Therefore, in the remainder of this discussion, the changes in carotid flow will be considered as being primarily due to changes in cerebral flow.

For accuracy, the carotid vascular resistance was measured over a wide range of pressures before, during, and after perfusion, and resistance was calculated and compared at similar pressure levels during these periods. This comparison at similar pressures is necessary, since a straight-line relationship between pressure and flow does not obtain for the cerebral vascular bed.

A striking fall in resistance was observed in all animals during perfusion and in 7 out of 10 dogs the resistance remained low after perfusion. Apparently, the cerebral vessels dilate during perfusion so that a disproportionate amount of the perfusion blood volume flows through the cerebrum.

Several factors could cause the marked lowering of the cerebral vascular resistance during perfusion. Since it has been shown that anoxia[1] produces a similar result, this could cause the changes observed. However, in all experiments, the oxygen saturation of the arterial blood was between 92 and 98 per cent, and consequently anoxia does not explain the observations. It has been shown by Eckstein[2] that hemoglobinemia produces coronary vascular dilatation. Hemoglobinemia, however, probably does not account for the changes in the cerebral vascular bed, for the amount of hemolysis was less than 70 mg. per 100 ml. in some of the dogs in which the greatest decrease in cerebral vascular resistance was observed.

As a result of Kety and Schmidt's[5, 6] monumental work on cerebral blood flow, it has been accepted that cerebral vascular resistance is controlled primarily by changes in carbon dioxide tension. They showed that hypocapnea caused by hyperventilation resulted in increased cerebral resistance and

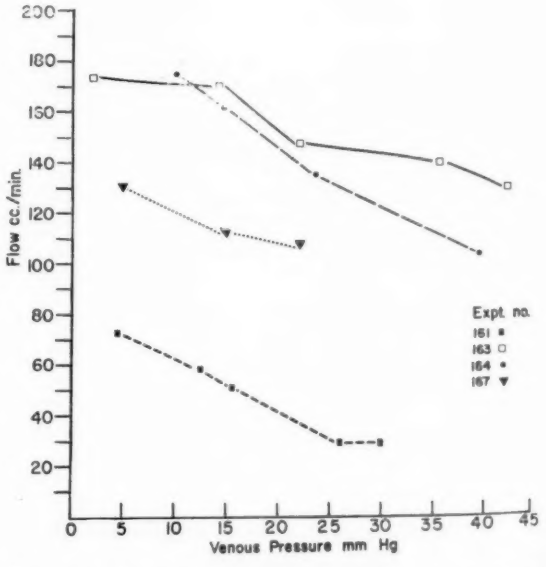

Fig. 3. Effect of increased superior vena cava pressure upon total carotid blood flow.

hypercapnea produced by breathing 5 or 7 per cent carbon dioxide resulted in decreased cerebral vascular resistance. Because the carbon dioxide tension was below 30 mm. Hg in these experiments, an increase in cerebral resistance and a decrease in flow would be expected according to Kety's observations. In reality, there was a marked fall in resistance with increased flow. Therefore, during perfusion, carbon dioxide tension probably does not play a part in the regulation of cerebral blood flow. This observation is further supported by the evidence that raising carbon dioxide tension had a variable effect upon cerebral vascular resistance. These findings are similar to those reported by Halley and associates[3] concerning carbon dioxide tension and cerebral vascular resistance during perfusion.

Cerebral vascular resistance fell in all experiments during perfusion and the blood pH fell also (Table I) as a result of a metabolic acidosis. These parallel, consistent changes raise the question of the possible effect of blood pH upon cerebral vascular resistance. Kety and colleagues[4] studied cerebral blood flow in patients with diabetic acidosis in whom pH and carbon dioxide tension were both low. In these cases, even though hypocapnea was present, cerebral blood flow was increased above normal and cerebral vascular resistance decreased. These findings are the opposite of what one would expect with hypocapnea per se. The observations are, however, quite similar to those described in our experiments and imply that reduced pH is perhaps a more important factor in the control of cerebral vascular resistance than carbon dioxide tension. Unfortunately, pH was not determined in all experiments after perfusion and any relationship between pH and return of cerebral vascular resistance to normal values during this period in 3 animals cannot be assessed.

These experiments also clearly show that increasing superior vena caval pressure above 10 mm. Hg has an adverse effect upon carotid blood flow and emphasize the importance of maintaining superior vena caval pressure within normal limits during perfusion in order to maintain maximum cerebral blood flow.

SUMMARY

1. Carotid blood flow was measured in 10 animals before, during, and after perfusion. In 6 animals blood flow through one carotid artery was monitored, and in 4 the total carotid flow was measured.

2. In all instances, carotid blood flow increased and cerebral vascular resistance fell during perfusion.

3. In 3 experiments, the cerebral vascular resistance returned to control levels after perfusion. In the other 7 animals, the resistance remained decreased.

4. Raising carbon dioxide tension from low to normal levels during perfusion resulted in variable and inconsistent changes in cerebral vascular resistance.

5. It was postulated that decreased cerebral vascular resistance during perfusion was primarily due to a lowered blood pH, and not to changes in carbon dioxide tension.

6. Increasing superior vena caval pressure above 10 mm. Hg results in a significant decrease in carotid blood flow.

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Some aspects of surgery for coronary disease

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It is a well-known fact that coronary arterial disease is responsible for a large per cent of the total mortality rate figure in our so-called modern and highly cultured countries.

In the United States recent statistics have shown that cardiovascular disease is responsible for more than half of the total deaths. Coronary arterial disease is the cause of about 20 per cent of the deaths in the cardiovascular group. This means that in the United States cardiovascular disease causes over 2,000 deaths per 1 million people each year. In Sweden the figures are somewhat lower. In a population of about 7.5 million, approximately 9,000 individuals die from coronary disease. This corresponds roughly to figures from England, where about 1,200 people in 1 million die from this cause. The United States is also leading in another respect, namely, that the incidence of morbidity and death from coronary arterial disease is increasing in the younger age groups more than in any other country in the world.

In Sweden, coronary patients occupy a large number of our hospital beds and a survey made by Biörck and Malmros from 13 big hospital centers showed that between 17 and 19 per cent of all hospital beds were occupied by such patients.

The mortality rate in coronary disease is not the only question of importance. Statistics have shown that about 25 per cent of patients with an acute coronary infarction die in their first attack. About 75 per cent of all patients survive their first attack but have more or less long-lasting, distressing, and disabling symptoms as a sequel. The mean length of life after the first infarction has increased during the last 30-year period and various statistics show that the increase has been from a little less than 4 years up to between 7 and 8 years (Fig. 1). This might be due in part to the improvement in modern medical treatment, such as the introduction of anticoagulant therapy. The majority of the patients who have survived die in new coronary attacks and only a relatively small number (about 10 per cent) die of other diseases. About one-third of the patients who survive their first attack never go back to work again. A little less than two-thirds of them go back to part-time and some even to full-time work. The most distressing symptom these patients suffer is angina pectoris.

Medical treatment, although prolonging life somewhat, has very little influence on the natural course of an already established occlusion in the main stem or in a major branch of a coronary artery.

It is, therefore, not at all astonishing that in connection with the rapid development of vascular surgery, surgical treatment of localized single obstructions of coronary arteries have come into the foreground in a large number of laboratories working experimentally with the problems of coronary arterial disease. The experiences from

The John Homans Memorial Lecture read at the Fourteenth Annual Meeting of the Society for Vascular Surgery, Miami Beach, Fla., June 12, 1960.

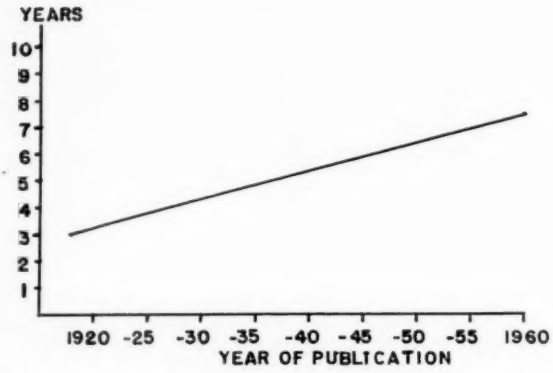

Fig. 1. Survival after first coronary occlusion.

such investigations are now being applied clinically.

The surgical treatment of more or less isolated well-localized coronary occlusions, which are the ones suitable for direct surgical attack, is possible because of the fact that the major branches of both the right and left coronary arteries are located under the visceral pericardium on the outside of the myocardial layer, and the fact that the arteriosclerotic processes are mostly localized to this part of the arteries. It is the secondary branches which penetrate into and give finer arteries to all parts of the muscular heart wall. Normally, there are very few or no collateral communications between the right and left coronary arteries. In large series of normal human hearts such anastomoses have been found to be present in between 8 and 9 per cent of the hearts examined. Very few small branches from arteries outside the coronary arterial system provide the normal myocardium with arterial blood. Such small branches have been demonstrated from both the phrenic and mammary arteries and from the small arteries in the walls of the aorta and pulmonary arteries. Both these small vessels, and the intercoronary anastomoses in particular, seem to be able to enlarge spontaneously and increase in number when the heart muscle needs an increased arterial blood supply, such as after a partial or complete coronary obstruction. The partial or even complete recovery after a coronary obstruction is due to the presence and development of such anastomoses. Postmortem studies have shown that there is a very marked increase in intercoronary anastomoses in severe cases of coronary obstruction and that such communications can develop rapidly in acute cases, even within a matter of a few days. Instead of being found in 8 to 9 per cent as in normal hearts, they may be found in almost 100 per cent.

As time has passed and we have gained more knowledge about Nature's own way of counteracting the effects of chronic coronary obstruction, plans have been made. As a result, many different surgical attacks are performed to help Nature provide the myocardium with an increased blood supply. Table I, taken from a Swedish article published in April, 1960, by Haeger, shows a résumé of different methods used both experimentally and clinically.

Concerning method I *A*, Claude Beck has performed a careful and critical work experimentally and tested it clinically. His clinical results show that patients with angina pectoris, whether it is in combination with a previous coronary infarction or not, who are operated upon with production of adhesions carrying vessels between the parietal pericardium and the myocardium have at least 3 times a better chance to survive after an acute coronary occlusion than patients of the same sort without operation. This is considered to be not only the result of an increase in arterial blood supply to the myocardium, but also the result of a more even arterial blood distribution to all parts of the myocardium, even if a new coronary occlusion should take place. Localized areas with low oxygen content bordering areas with high oxygen content are thus avoided and the risk of ventricular fibrillation minimized.

An enormous amount of experimental work has been done with method I *B*, but clinical application of the experimental experiences has not been satisfactory and all these methods are, at the present time, more or less abandoned. The same holds true for the methods I *C* and I *D*, in which arterialization of the myocardium directly from the

various arteries which have been implanted into it has been tried. From these arteries and even from the aorta prosthetic tubes have also been implanted with the hope that they would stay open and not close down to the same extent as the implanted arteries tend to do. The results have not been very good and with few exceptions these methods are now not in extensive use.

The attempt to achieve improvement by reduction of the metabolic rate and by neurological operations (methods II and III) has now more historical than current interest.

Table I. *Surgical methods for correction of coronary insufficiency*

I. To produce extracardial revascularization
- *A. From the pericardium*
  1. Mechanical abrasion of the parietal and visceral pericardium
  2. Introduction of foreign material in the pericardium (talcum-asbestos)
- *B. From other sources*
  1. Suturing of mediastinal tissues directly to the pericardium
  2. Suturing of omentum directly to the myocardium
  3. Suturing of pedicled mucosa-deprived stomach flap to the myocardium
  4. Suturing of pedicled mucosa-deprived jejunal flap to the myocardium
  5. Suturing of pedicled skin graft to the myocardium
  6. Bilateral mammary artery ligation
- *C. From arteries implanted directly in the myocardium*
  1. Mammary artery
  2. Carotid artery
  3. Subclavian artery
- *D. From prosthetic tubes*
  1. Between mammary artery and myocardium
  2. Between the aorta and the myocardium
  3. Between the left ventricle directly to myocardium

II. By reduction of the metabolic processes
- *A. Surgical subtotal thyroidectomy*
- *B. Radioactive thyroidectomy*

III. Symptomatic neurosurgical interventions
- *A. Vagotomy*
- *B. Different types of sympathectomy*

IV. Surgical procedures on the coronary vessels
- *A. Resection of coronary artery and end-to-end anastomosis*
- *B. Restriction of the coronary sinus flow*
- *C. Reversion of the coronary sinus flow*
- *D. Coronary endarterectomy*
- *E. Coronary artery incisions and autogenous patch transplantations*

The last (IV) of surgical methods being tried is that of direct attack on the coronary vessels themselves. Twenty years ago Gordon Murray of Toronto showed that resection of a segment of a coronary artery and suture end-to-end was possible with good function of the anastomosis. The operation, however, took a long time and resulted in myocardial infarction. Since the introduction of perfusion techniques, Thal and associates and others have repeated such coronary resections experimentally. After some period of time, only 7 out of a group of 17 surviving dogs had open anastomoses. Only a very short and localized stenotic area in a coronary artery without open myocardial branches within the resected segment could be considered for this type of operation. Because of the experimental results with a very high per cent of restenosis at the site of the anastomosis, this type of operation does not seem to be recommendable.

For arteriosclerotic occlusion processes, endarterectomies have been performed in cases of peripheral arterial disease for quite some time and with reasonably good results. It is, therefore, no wonder that this type of operation was taken into use for arteriosclerotic coronary constrictions. May worked out the technique and Bailey improved upon it, as well as Longmire and Cannon, who reported some time ago having operated upon 10 human patients with 5 survivals.

Since some years back the interest in coronary disease has been very high and one of the main problems for research in our laboratory. It is my associate, Senning, who has been leading this work both experimentally and clinically. By different means localized partial occlusive processes have been produced in the coronary arteries of dogs and these have subsequently been attacked in 2 different ways. Senning started out by performing endarterectomies. It was, however, found that secondary branches in the area of endarterectomy were sealed off by their ruptured intima which rolled in and by secondary thrombotic processes

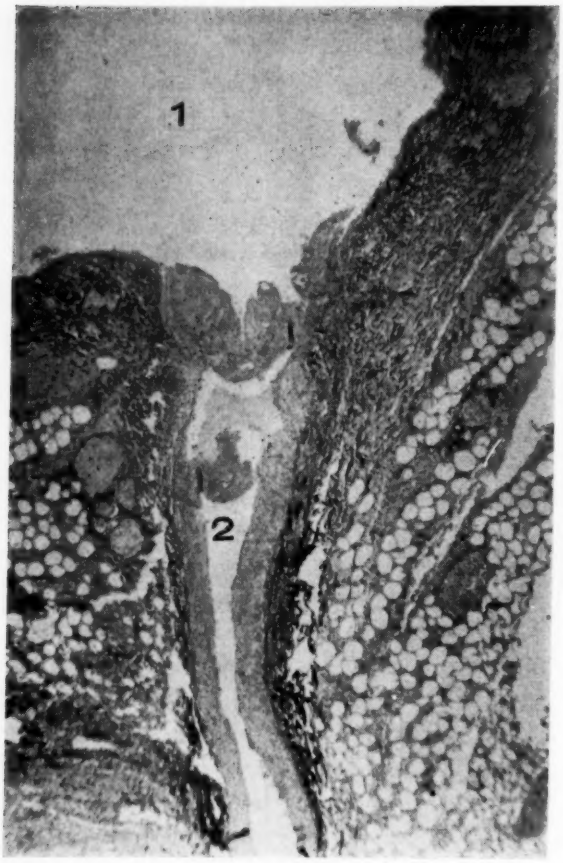

Fig. 2. *1,* Lumen of endarterectomized coronary artery. *2,* Side branch of coronary artery.

Fig. 3. *1,* Aorta. *2,* Main stem of left coronary artery. *3,* Circumflex branch of coronary artery with patch graft (5 months after patch grafting).

formed at this point. The same thing was also noted at postmortem examination in a human subject who died shortly after the endarterectomy (Fig. 2). After such operations the big arteries which were endarterectomized had a good internal surface and were patent. But the blocking-off of several myocardial branches was certainly a very disadvantageous side effect.

Senning, therefore, had the idea that one ought instead try to open up the narrow part of the coronary artery longitudinally, under direct vision peel out the most marked and eventually calcified portions of the intima (avoiding touching the intimal areas of the open side branches), and then enlarge the lumen of the open artery by inserting a strip of autogenous vessel as a patch graft in the incision. A piece of the dog's opened mammary artery was used in these experiments.

A series of dogs were operated on in this manner. Fig. 3 demonstrates such a graft inserted in the circumflex branch of the left coronary artery 5 months after operation and Fig. 4 shows such a graft in the anterior descending branch of the left coronary artery after the same length of time. Selective coronary angiograms and also histologic examinations showed good healing into the arteries of these patch grafts.

Parallel to these experimental operations, work has also been going on to refine our methods of coronary angiography, as an exact diagnosis was considered to be necessary for selection of patients suitable for grafting. The head of our x-ray department in the thoracic clinics, Dr. Nordenström, and his associates, have, with the help of the experimental department of the Elema Factory in Stockholm, worked out a system of 4 x-ray tubes working in pairs in 2 planes at right angles to each other. One tube in a pair exposes in one plane, at only a slightly different angle from the other, practically simultaneously (with only $\frac{1}{100}$ of a second apart) one film each of the rapidly moving roll film. In such a manner beautiful stereoscopic pictures are obtained and a comparison of the stereoscopic pictures in the

2 planes at right angles to each other gives considerably more information than the usual pictures in the evaluation and localization of different arterial narrowings.

One human subject has been operated on with autogenous patch graft from the major saphenous vein 8 months ago with an excellent immediate result. We wanted, however, to follow both the clinical development and anatomic result in this case before starting to treat cases of this sort in series and it is therefore presented more in detail.

The patient was a 55-year-old man who had been increasingly disabled since 1955 because of precordial, radiating, and progressively severe anginal pain produced by physical activities, emotional causes, eating big meals, and exposure to cold. In 1956 and 1958 he was hospitalized for about 2 months each time for acute severe attacks of pain, the first time with objective signs of myocardial infarction. He had been treated in the usual way medically and also with long-term anticoagulant therapy.

At no time had there been objective signs of cardiac decompensation. Essentially, blood pressures were within a normal range but close to the upper limits. The heart was of normal shape and only slightly increased in size. The man had normal heart rhythm with the exception of short bouts of extrasystole arrhythmia with long intervals. The electrocardiogram showed slight left axis deviation. There were signs of left ventricular conduction trouble. There were pronounced signs of generalized coronary insufficiency. Measured work on the bicycle ergometer was impossible to test because merely the movements on the cycle without resistance produced severe anginal pain.

Coronary angiography (Fig. 5, *A*) showed diseased walls of the right coronary artery and an unusually early dividing of this artery in its smaller myocardial branches, which went over in a fine network of vessel branches, evidently anastomosing with peripheral branches on the left side. The left coronary artery was slightly narrowed, even at its aortic orifice. At the point of ramification of the anterior descending and circumflex branches there was a slight narrowing. The anterior descending branch was considerably narrowed, about 2 cm., in a peripheral direction and further out was not visible.

The circumflex branch was in its first centimeter moderately stenosed, but then there was a 1 cm. very pronounced narrowing followed by a practically normal width. The patient had thus comparatively localized constrictive lesions which were deemed suitable for patch grafting. Operation was performed under Pentothal induction and Flouthane-Celocurin anesthesia. The Aga automatic double pump was used with bypass, left auricle to femoral artery and right auricle to pulmonary artery. The patient's own lungs served as the oxygenator. With a heat exchanger on the side of the left pump, the patient's temperature was brought down to 27° C. During this time the main stem, the anterior descending and the circumflex branches, and their side branches were dissected and encircled by sling ligatures. When these were tightened, the heart went into ventricular fibrillation and stayed

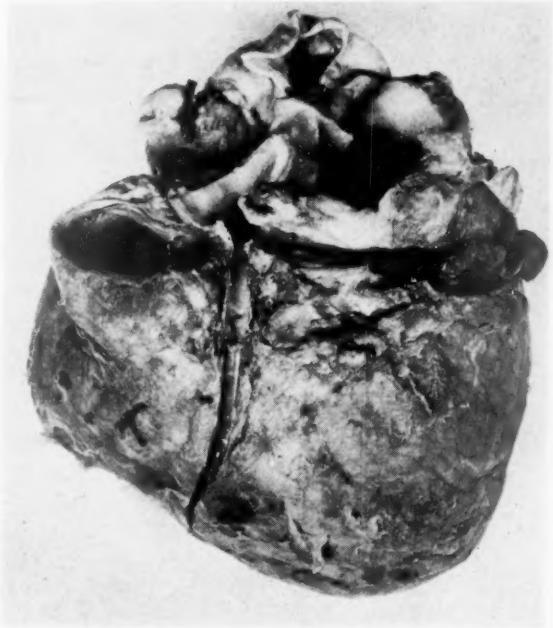

Fig. 4. Patch graft in previously strictured descending branch of left coronary artery (5 months after patch grafting).

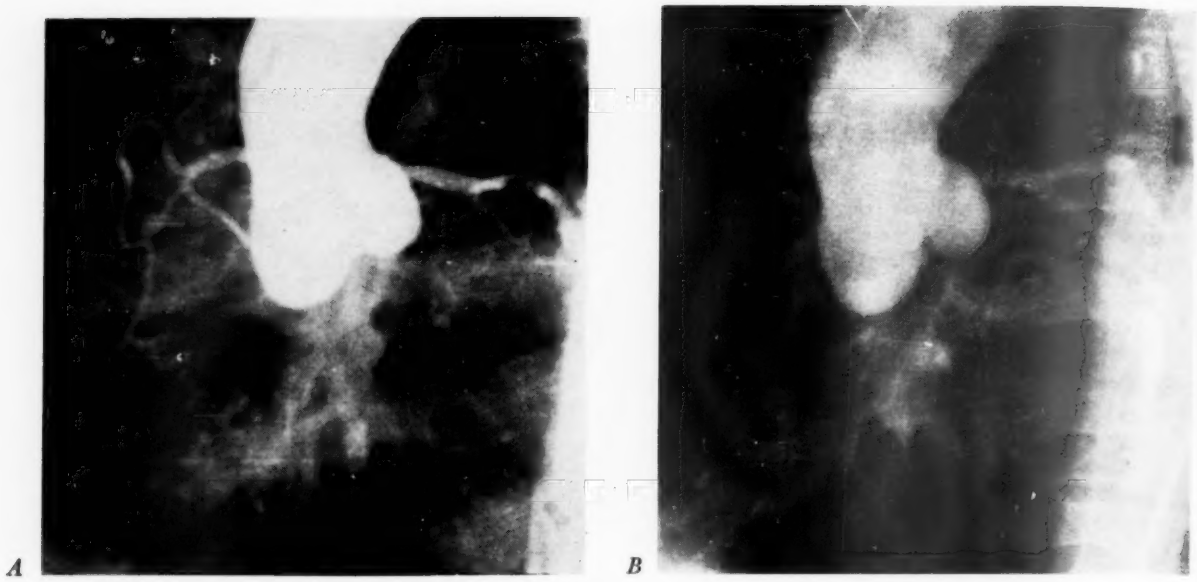

Fig. 5. *A*, Right coronary artery (*1*) and left coronary artery (*2*). *B*, Main stem of left coronary artery (*1*), descending and circumflex branches cylindrically widened 5 months after patch grafting (*2* and *3*).

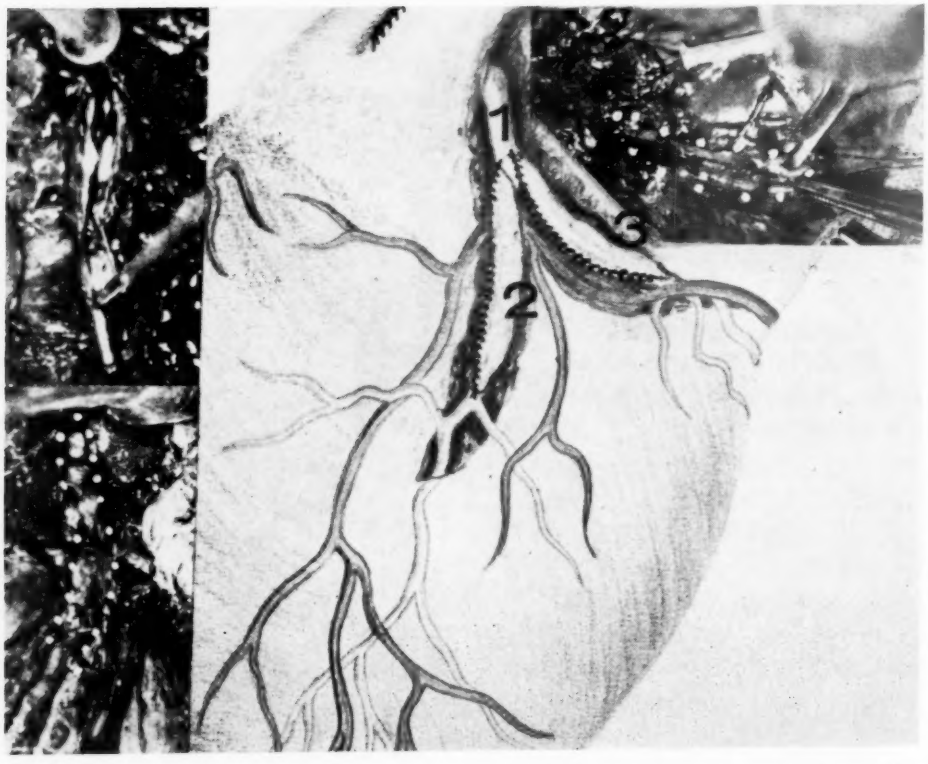

Fig. 6. Schematic drawing shows *1*, main stem of coronary artery, *2*, descending branch, and *3*, circumflex branch. Right and left inserts are operative photographs.

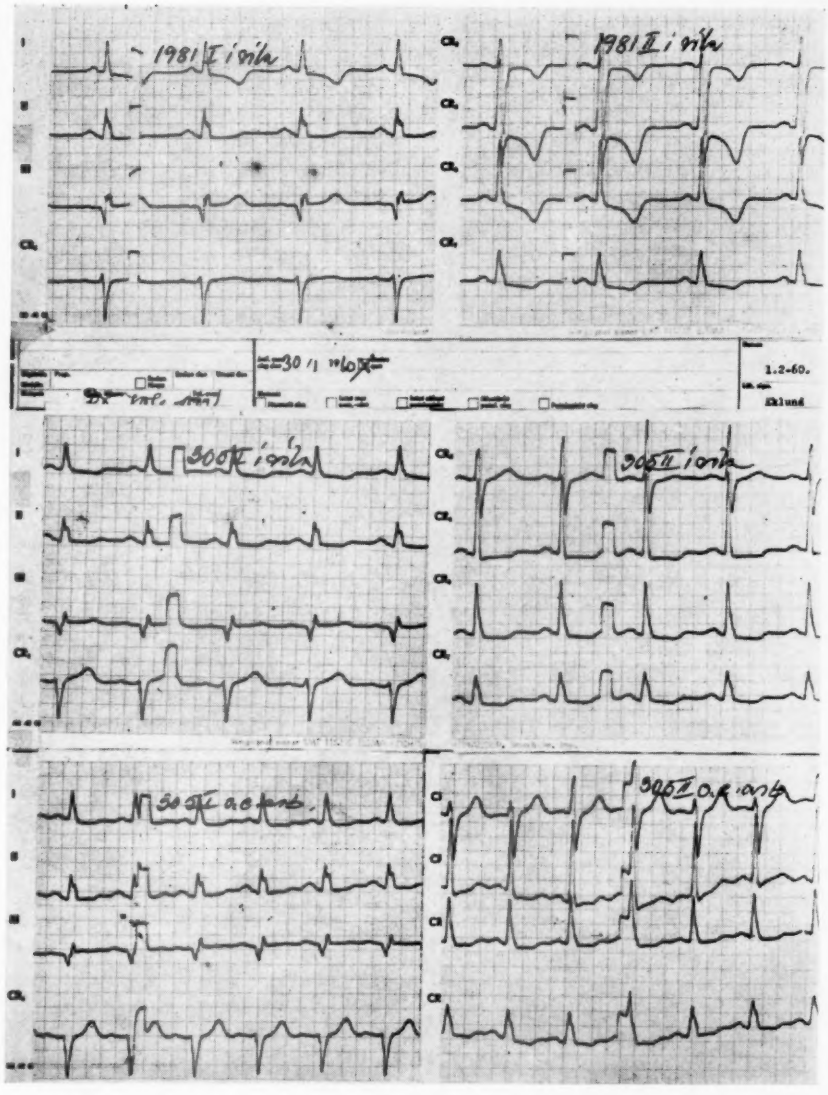

Fig. 7. Electrocardiograms of patient whose case is discussed.

so for a little more than 2 hours. In the anterior descending artery a 4 cm. longitudinal incision was made from a few millimeters central to the origin from the main stem of the coronary artery. Some gross intimal sclerotic areas, partly calcified, were peeled out, with avoidance of the parts of the intima surrounding side vessels. A piece of the wall of the patient's own saphenous vein, taken out close to the ankle, was trimmed in both ends and sutured into the incision of the descending anterior artery branch. In the wall of the circumflex artery a 3.5 cm. long incision was made and was treated in the same way. A similar patch graft was sutured into place with a No. 6-0 Deknatel silk suture. Before the proximal end of the incision was closed an atheromatous plaque was also peeled out from the aortic orifice of the main left coronary artery (Fig. 6).

The heat exchanger was now switched over for rewarming and, when the esophageal temperature which had been kept round 23° C. during the long operation was up to 28° C., the heart was defibrillated with one electric shock. The bypass pump on the right side was detached. When the temperature in the esophagus was 34° C. and in the rectum 28° C. the left pump was

also detached. In the meantime the left side of the heart had been kept decompressed by the left pump and was only gradually permitted to take over. The total time for bypass including cooling, the coronary operation, and rewarming was close to 3 hours. When the left pump was detached the peripheral arterial blood pressure was within normal limits and remained so during the whole postoperative period. The patient woke up rapidly and there were no postoperative complications.

About 4 months postoperatively the patient was hospitalized and re-examined. He never had any anginal pains after his operation, and he had already started part-time work after having been completely disabled before his operation. The electrocardiogram had improved markedly. On the top of Fig. 7 the preoperative readings are seen. The reading in the middle was taken at rest, 3 months after operation, and the lowest one after measured physical work. The electrocardiogram had been very much improved. The physical working capacity had increased and the patient tolerated on the bicycle ergometer 200 kilogram-meters per minute for 6 minutes with an increase in pulse frequency to 140 per minute and 400 kilogram-meters per minute for 6 minutes with only 154 pulse beats per minute. During or after this work he had no anginal pains or any other subjective complaints except that his legs felt tired. The electrocardiogram did not change during the work.

Postoperative coronary angiography (Fig. 5, *B*) showed 2 grafts in V-form just proximal to the dividing point on the left coronary artery, one attached to the anterior descending branch and one to the circumflex branch, each cylindrically widening these two arteries where before they had been nearly occluded. Some side branches in these areas were also visible. We have, therefore, now come to the conclusion that this method of operation is to be recommended for further trial in this type of patient.

An experimental study of thoracic transposition of the spleen: a method of portal decompression

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In 1955 two Finnish surgeons, Nylander and Turunen,[6] reported the treatment of 3 patients with portal hypertension and recurrent esophageal hemorrhage by transposition of the spleen into the left pleural cavity. This operation was first performed in November, 1952. In 1959 Turunen and Laitinen[7] described the case of an additional patient and gave a follow-up report on the earlier patients. Splenoportograms, performed 8 months to 5 years after splenic transposition, showed numerous splenothoracic venous collaterals. Esophageal varices had either disappeared or decreased markedly in size. There had not been a single instance of recurrent major esophageal hemorrhage.

Nylander and Turunen first conceived the idea for this procedure after treating a patient with a traumatic rupture of the diaphragm and displacement of the spleen into the left side of the chest. Venous collaterals between the spleen and thoracic wall were so extensive that it was not possible to restore the spleen to the abdomen and splenectomy had to be performed. The magnitude of the venous collaterals was so impressive that the doctors thought such collaterals might prove useful in the treatment of portal hypertension. The clinical results subsequently obtained seem to substantiate this view.

Read at the Fourteenth Annual Meeting of the Society for Vascular Surgery, Miami Beach, Fla., June 12, 1960.

These data suggested that it would be worth while to conduct an experimental evaluation of the effects of thoracic transposition of the spleen. If the procedure could be demonstrated to be both safe and effective in decompressing an obstructed portal venous system, it would be a useful addition to the present surgical armamentarium for the treatment of portal hypertension. It might provide a logical alternative to a portal systemic venous shunt in poor-risk patients and prove to be the procedure of choice for patients in whom a shunt is not possible.

There are two previous reports of experimental studies of thoracic transposition of the spleen. In 1957 Turunen and associates[8] reported that transposition of the spleen into the left pleural cavity of dogs resulted in prompt development of abundant splenothoracic venous collaterals. Early in 1960, Hoffman and Freedlander[4] confirmed this observation and reported the additional finding that in dogs with thoracic transposition of the spleen it was possible to ligate the portal vein acutely and achieve survival of more than 50 per cent of the animals. The latter authors also described their experiences with 3 clinical cases.

Our studies were performed in an effort to obtain more information on this subject.

METHODS

Adult mongrel dogs weighing 6 to 15 kilograms were used. The operative procedures were performed with intravenous

pentobarbital anesthesia (30 mg. per kilogram). An endotracheal tube and mechanical respirator were used in all the thoracic procedures. The animals were fed standard rations and water ad libitum throughout the preoperative and postoperative periods.

A standard method for thoracic transposition of the spleen was employed throughout the study. An anterolateral thoracotomy through the eighth or ninth intercostal space was used and an incision was made in the diaphragm extending from its central tendon to the posterolateral chest wall. The spleen was delivered into the pleural cavity and all the attachments except for the main splenic artery and vein were ligated and divided. Care was taken to avoid torsion of the pedicle. The diaphragm was closed loosely around the splenic pedicle with interrupted silk sutures. The spleen was placed so that its convex surface lay against the anterolateral chest wall. In some animals parietal pleurectomy was performed over the area in contact with the spleen. Splenic pulp pressure was measured before the chest was closed. The animals were divided into 5 groups.

Group I. In 15 animals the spleen was transposed into the left pleural cavity by the method described.

Group II. In 26 animals the spleen was transposed into the left pleural cavity and 1 week later the splenic vein was ligated. In Fig. 1 the site of splenic vein ligation is shown: care was taken to preserve the communication between the splenic vein and the gastric vein.

Group III. In 5 animals all the steps for transposition of the spleen into the chest were carried out but the spleen was then returned to the abdomen and the diaphragm closed. One week later the splenic vein was ligated.

Group IV. In 7 dogs the lumen of the thoracic inferior vena cava was constricted approximately 50 per cent by a ligature and the spleen was transposed into the left pleural cavity. These procedures were performed simultaneously through a left anterolateral thoracotomy.

Group V. In 11 animals from Group II the postoperative splenograms ultimately showed extensive communication between the splenic vein and portal vein. This communication was primarily via the gastric vein (Fig. 1). After this demonstration in the 11 animals, the portal vein was acutely ligated.

Postoperative studies. After operation in each animal splenograms and portograms were performed periodically and at the same time splenic pulp and portal vein pressures were measured with a saline manometer. These procedures were performed under direct vision at thoracotomy or laparotomy. Manual injection of 15 c.c. of 50 per cent Hypaque or 70 per cent Urokon was routinely used for the contrast study. Hematologic studies were performed at frequent intervals in the postoperative period in each animal. In 5 animals from Group II control values for the hematocrit, platelet count, white cell count, and differential white cell counts were obtained preoperatively and again on the first, seventh, eighth, ninth, fifteenth, thirtieth, and sixtieth postoperative days. Roentgenograms of the chest were obtained periodically in the follow-up period.

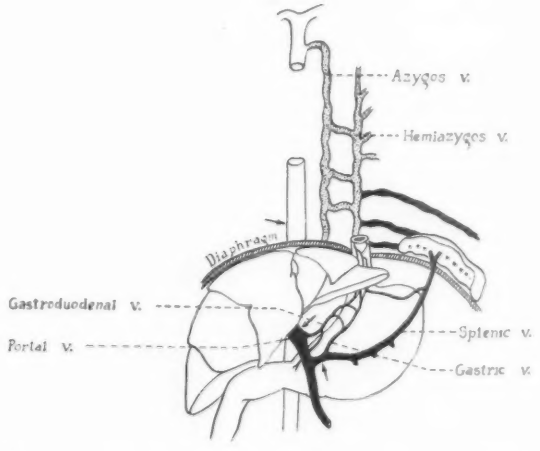

Fig. 1. Diagram of the spleen in the left pleural cavity. The intercostal veins are shown connecting the splenic venous drainage to the azygos veins. The arrows represent the sites of ligation of the veins in various phases of this study.

RESULTS

The general response to thoracic transposition of the spleen. In 41 animals transposition of the spleen into the left pleural cavity was the sole initial operation (Groups I and II). From these animals data concerning the general response to thoracic transposition of the spleen were obtained. No special postoperative care was given. Thirty-two animals (78 per cent) survived the operative procedure and became a part of the long-range study. Nine animals (22 per cent) died in the early postoperative period. The causes of death were ascribed to hemothorax (2), empyema (2), splenic infarction (1), pneumonia (2), and anesthesia (2).

Follow-up studies on the survivors showed that the general health of the animals remained good and there was no clinical evidence of any deleterious effects of transposition of the spleen into the chest.

Hematologic response. The hemograms remained essentially normal over the long-range period with some variation at specific intervals. A leukocytosis (20,000 to 30,000 white blood cells) often developed after an operative procedure (transposition, splenic vein ligation, or splenoportography) but this promptly returned to normal in the following weeks. The differential white cell count revealed a shift to the left at the time of the leukocytosis but otherwise remained within normal limits. The hematocrit stayed within a normal range. Ligation of the splenic vein was usually followed by a transient fall in the platelet count but never below the range of normal. These observations also apply to the 5 animals in Group II which had more detailed hematologic studies.

Roentgenograms of the chest. In each animal in the first few days after transposition of the spleen about 30 per cent of the left hemithorax became roentgenographically opaque. Within 10 days this opacity began to diminish and ultimately involved only 10 to 15 per cent of the left side of the chest (Fig. 2). There were no cases of pleural effusion, demonstrable atelectasis, or pneumonitis in the long-range follow-up period.

Tissue studies. In the first several weeks, direct observation of a nonadherent portion of the spleen showed a mottled white splenic capsule, the picture of so-called "perisplenitis." Most of the splenic surface developed adhesions to surrounding structures—diaphragmatic, visceral, parietal, or mediastinal pleura or the chest wall (Fig. 3). The hilar region of the spleen characteristically developed dense adhesions to the diaphragmatic pleura and chest wall. The adhesions were usually thick and fibrous. As a general rule, one surface, one edge, or a portion of the splenic surface was found to be entirely free of adhesions. However, most of the available splenic surface was densely adherent to surrounding structures. The number and magnitude of the adhesions increased over a period of several months.

The gross response of the spleen itself to thoracic transposition varied considerably. In some animals there was a moderate diminution in the size of the spleen, whereas in others this was slight or imperceptible. Macroscopically the splenic pulp maintained a normal color and architecture. Microscopic study showed a thickening of the splenic capsule and a mild to moderate fibrosis of the pulp. The junction between the spleen and lung or spleen and chest wall demonstrated a fibrous layer containing numerous vascular channels (Fig. 4). On study of the union between the lung and the spleen a thin layer of atelectasis adjacent to the fibrous layer was found. This was followed by a transitional zone of pulmonary tissue with thickened, edematous alveolar walls which blended into normal lung. Vascular channels directly connecting the spleen and lung were not demonstrated. The remainder of the left lung appeared normal both macroscopically and microscopically.

The results in the specific groups.

Group I (transposition of spleen). Of the 15 animals in this group 3 died in the immediate postoperative period and 12 survived. The survivors have been followed for from 3 to 4 months. Splenothoracic venous collaterals, draining into the azygos system,

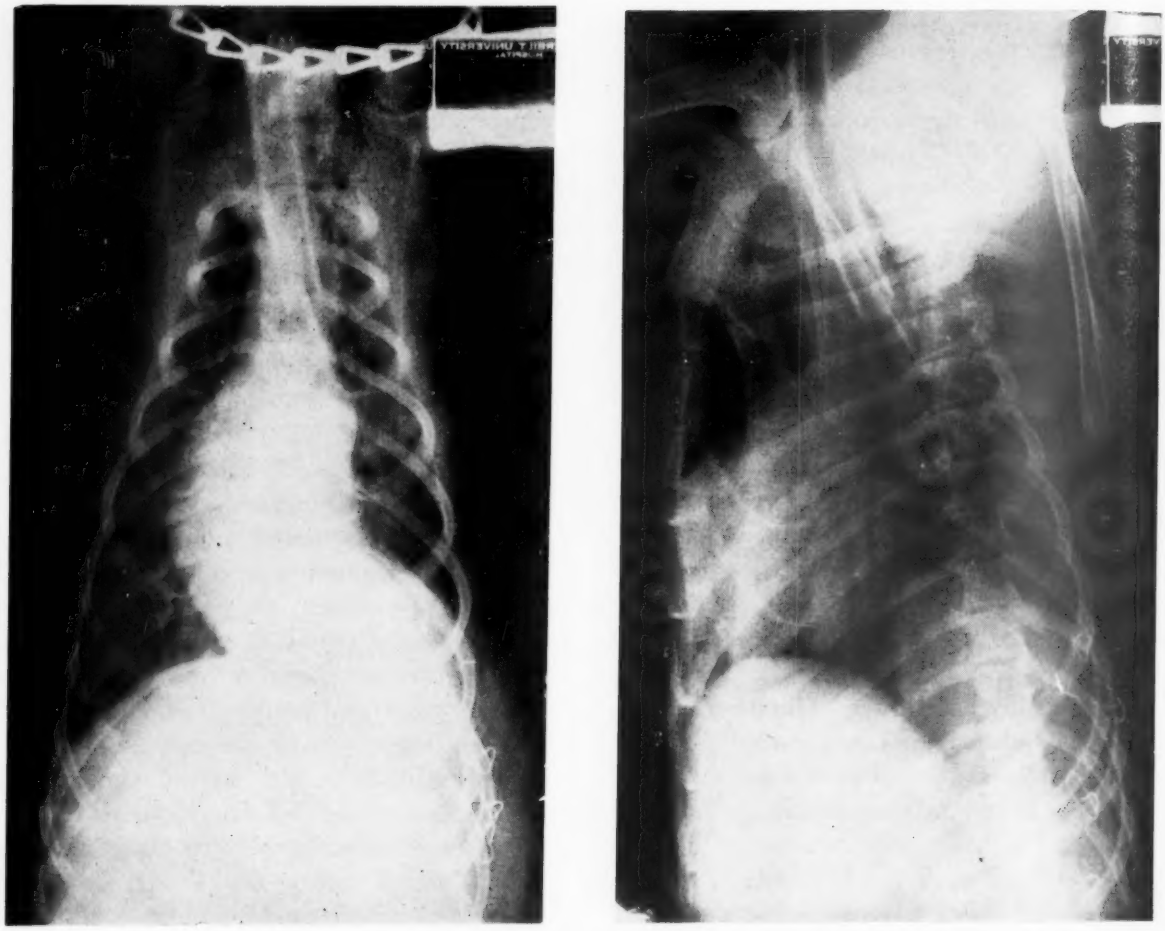

Fig. 2. Roentgenograms of the chest of a dog 5 months after thoracic transposition of the spleen. The oblique view gives a good indication of the amount of space the spleen occupies.

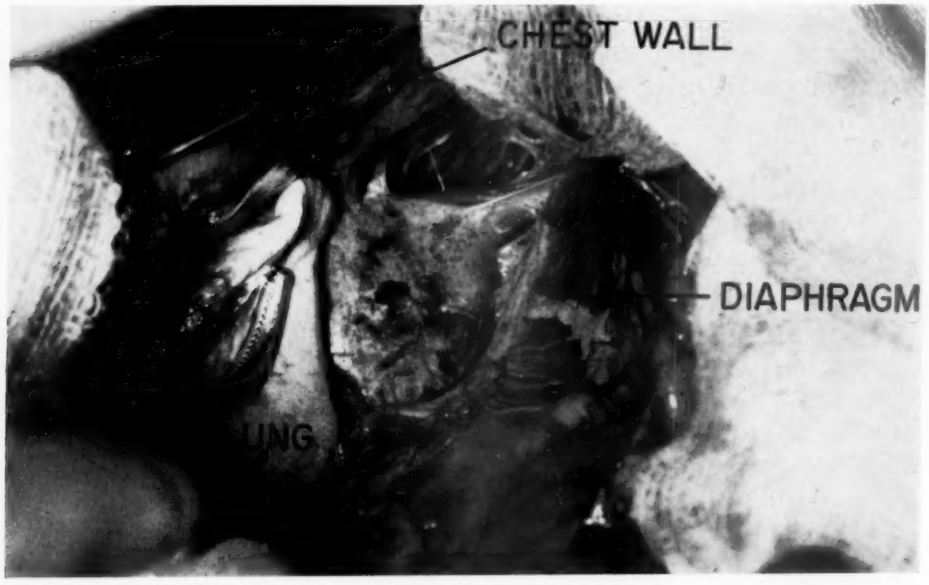

Fig. 3. The findings at exploratory thoracotomy in a dog 6 months after the spleen had been transposed into the left pleural cavity. Note the mottled splenic capsule and the dense fibrous adhesions between the spleen and surrounding structures.

were demonstrable on the first splenogram performed 2 weeks after transposition of the spleen (Fig. 5). Subsequent splenograms showed progressive development of splenothoracic venous anastomotic channels. Portograms demonstrated communication between the portal venous system, the spleen, and the splenothoracic collaterals.

Group II (transposition of spleen and subsequent ligation of splenic vein). Of the 26 animals in this group 6 died in the immediate postoperative period and 20 survived. The survivors have been followed for from 9 to 11 months. In the survivors, after the spleen had been in the left chest for 1 week, the splenic vein was ligated centrally. This was done to produce an elevation in the splenic vein pressure. Communication between the splenic vein and portal vein via the gastric and gastroduodenal venous system was undisturbed (Fig. 1). After the ligation the splenic venous pressure rose immediately from preligation levels of 8 to 15 cm. H_2O to 25 to 40 cm. H_2O. One week thereafter a splenogram was performed. At this time the splenic pulp pressure measured 7 to 16 cm. H_2O and remained in this range on subsequent examinations. The first splenogram (2 weeks posttransposition) showed splenothoracic collaterals in every animal (Fig. 6). Thereafter each splenogram demonstrated a progressive increase in the number and size of these splenothoracic anastomotic communications (Fig. 7). There was usually some filling of the portal system via the gastric veins and this increased with subsequent splenograms in several of the animals, however, the major drainage remained via the splenothoracic collaterals to the azygos system. There was no evidence of filling of the veins of the esophagus on any of the examinations. There was moderate narrowing of the splenic vein at the level of the diaphragm in a few animals. However, the subdiaphragmatic segment of the splenic vein invariably filled at the time of splenography.

Group III (controls). In these 5 dogs the spleen was delivered into the left side of the chest, all attachments were divided except the major artery and vein, and the spleen was returned to the abdomen. One week later the splenic vein was ligated. A striking change followed the central ligation of the splenic vein. The splenic pulp pressure rose from the normal range of 8 to 17 cm. H_2O to 30 to 50 cm. H_2O and the spleen became engorged and tense. One week later the splenic pulp pressure had returned to a normal range, the engorged spleen was decompressed, and there were numerous adhesions between the spleen and the omentum. Periodic splenograms showed collateral venous channels between the spleen and the omental veins. The most common route of splenic venous drainage, however, was from the splenic vein to the gastric and gastroduodenal veins and thence to the portal vein (Fig. 8). The entire venous blood flow from the spleen drained into the portal vein and

Fig. 4. Photomicrograph which shows junction between spleen and lung. The spleen had been transposed into the chest for 6 months. Note the normal architecture of the spleen, the thick fibrous layer at the zone of junction between spleen and lung containing vascular channels, and the thin layer of atelectasis adjacent to the fibrous layer. (×25; reduced ⅖.)

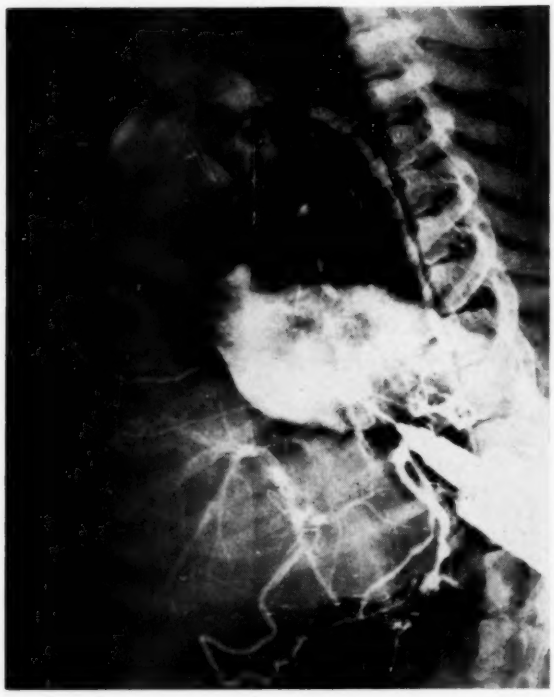

Fig. 5. Splenogram taken 2 weeks after transposition of spleen into left pleural cavity in a Group I animal. The azygos vein is well demonstrated. Intercostal veins are shown joining the internal mammary vein anteriorly. The portal vein is partly filled.

Fig. 6. Splenogram taken 2 weeks after transposition of the spleen into the chest in an animal from Group II. The splenic vein had been ligated for 1 week. Note the very large splenic shadow, also the pericardiophrenic and azygos veins.

there was no evidence of communication with the azygos system or with esophageal or supradiaphragmatic veins. A large nest of dilated veins developed in the splenic hilum in these animals (Fig. 9).

Group IV (transposition of spleen and constriction of inferior vena cava). In these 7 animals the lumen of the thoracic inferior vena cava was constricted by 50 per cent and simultaneously the spleen was placed in the left side of the chest. Three animals died in the early postoperative period and 4 animals survived and have been followed for 7 to 8 months. The amount of constriction of the thoracic inferior vena cava which was carried out in these dogs has been previously reported to produce ascites within 4 weeks.[4] Only 1 animal of this group developed ascites. Splenic pulp pressures measured before and after constriction of the thoracic inferior vena cava showed no appreciable change. Subsequent splenic pulp pressures were within the normal range. Splenothoracic venous anastomotic channels developed in all of the animals. However, there was one striking difference in this group. The spleen became adherent to the mediastinal structures at the site of exposure of the thoracic inferior vena cava, and the major venous collaterals shown by splenography were between the spleen and mediastinal veins, chiefly the pericardiophrenic and internal mammary veins (Fig. 10). There was only faint visualization of the azygos system.

Group V (transposition of spleen with splenic vein ligation and subsequent ligation of portal vein). These were 11 animals from Group II in which it was noted on splenography that the communication between the splenic vein and portal system, via the gastric vein, had become quite extensive. The spleen had been in the left hemithorax for from 4 to 6 months. These 11 animals were subjected to acute ligation of the portal vein (Fig. 1). The ligation was followed by a

rise in portal pressure from the normal levels of 7 to 17 cm. H_2O to 40 to 90 cm. H_2O. The small intestine characteristically became congested and somewhat cyanotic. Three animals, in which the portal pressure had risen above 70 cm. H_2O, died within a few hours after the operation. The remaining 8 animals (73 per cent) survived and in these dogs the portal pressure did not exceed 70 cm. H_2O. Subsequent portograms showed shunting of the portal venous blood through the spleen into the splenothoracic collaterals and hence to the azygos system. Portal vein and splenic pulp pressures returned to a normal range (Fig. 11). In some animals this appeared to be a rather complete shunting of the portal flow, while in others a moderate amount of the contrast medium reached the intrahepatic portal system via collaterals around the portal vein ligature. The animals with the more complete "portal-splenic" shunts became emaciated and wasted. They resembled dogs with portocaval shunts in which the portal flow has been completely diverted from the liver. On the other hand, the animals in which a moderate amount of the portal blood flow passed through the liver have maintained their weight and remained healthy.

The nature and extent of splenothoracic venous anastomotic communication after thoracic transposition of the spleen. In all the animals with thoracic transposition of the spleen collaterals developed promptly and were so extensive after 1 month that splenography usually gave a simultaneous angiocardiogram. The collateral channels were larger and more extensive in the animals in which transitory elevation of splenic or portal venous pressure was induced (Groups II and IV). The majority of the collateral venous channels drained into the azygos and hemiazygos systems. The largest and most impressive of the intermediary channels were the intercostal veins (Fig. 12). Other channels frequently seen on splenograms included phrenic veins, pericardiophrenic veins, internal mammary veins, and a variety of unidentified veins (Fig. 13). The most striking characteristic, common

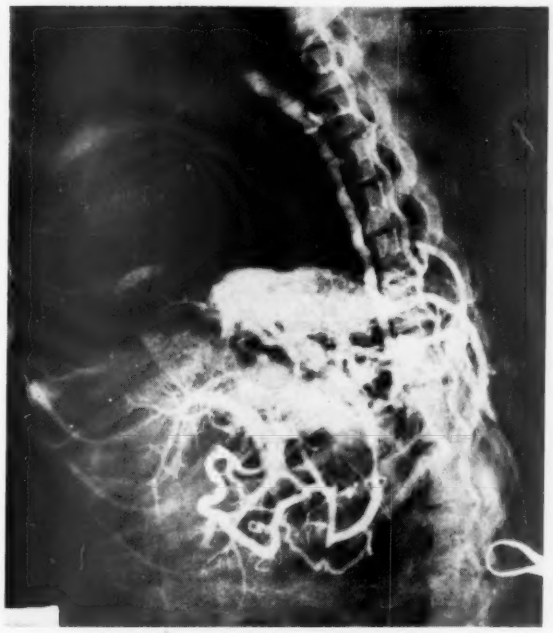

Fig. 7. Splenogram taken 2 months after thoracic transposition of the spleen in an animal from Group II. Note the azygos, hemiazygos, and intercostal veins. There are some unidentified veins connecting the spleen and the azygos vein. The splenic vein is narrowed at the level of the diaphragm. Note the portal vein filling.

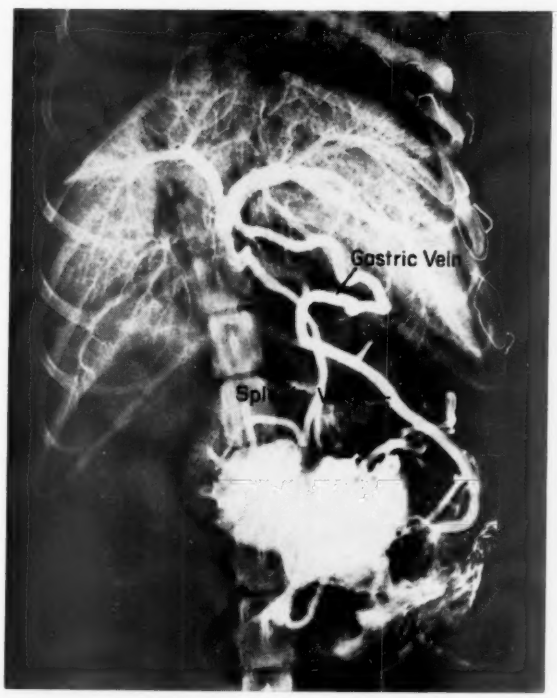

Fig. 8. Splenoportogram in a Group III animal taken 1 month after spleen was placed in the chest and then returned to the abdomen. Note collaterals to portal system and absence of any evidence of filling of the azygos systems.

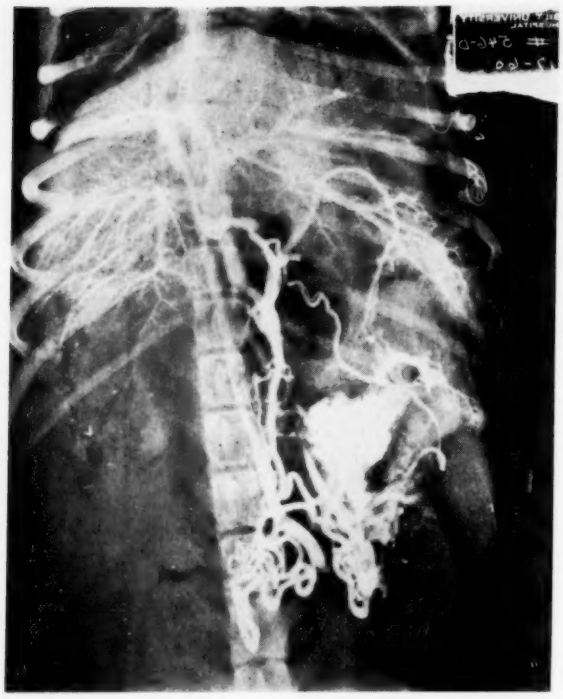

Fig. 9. Splenoportogram in a Group III animal taken 3 months after mobilization of the spleen. Note the tortuous nest of veins in the splenic hilum.

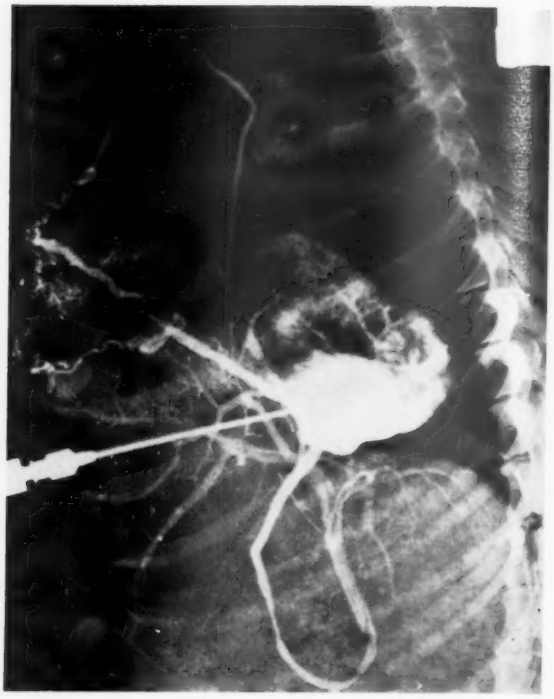

Fig. 10. Splenogram in a Group IV animal. Pericardiophrenic vein and early filling of internal mammary vein are shown, as is the communication to the portal vein via the splenic vein.

to the vast majority of the splenograms, was a large azygos vein filled with contrast medium. This vein was usually as large as the canine portal vein. The pericardiophrenic and internal mammary venous channels were very prominent in some animals, especially in the animals of Group IV (Fig. 14). In several animals a large phrenic vein ran from the splenic hilum along the superior surface of the diaphragm and drained directly into the thoracic inferior vena cava (Fig. 15). Each successive splenogram showed filling of new and different collateral channels and after 10 months there was no evidence that this process had ceased or reached a plateau. Another striking characteristic of splenic venous collateral formation is the presence of a large nest of veins in the splenic hilum.

COMMENT

The objective of this study was to determine whether thoracic transposition of the spleen was both safe and effective as a method of decompressing an obstructed portal venous system and, more specifically, to learn something of the nature and extent of splenothoracic venous anastomotic communications that follow this procedure. The operative mortality rate in this study of thoracic transposition of the spleen in the dog was 22 per cent. Seventy-eight per cent of the animals survived the procedure without the benefit of special postoperative care. One item of special interest was the development of pleural empyema in 3 animals. This probably was the result of faulty sterile technique. However, the bacterial flora of the canine spleen is unknown as far as we can discern. Like the canine liver, the spleen may harbor bacterial pathogens. Studies are now underway to determine the bacteriologic status of both the canine and human spleen.

The late results indicate that the thoracic spleen was well tolerated. The hematologic

studies revealed no untoward response. There were no pleural effusions and no evidence of significant compromise of pulmonary function. The thoracic spleen maintained a reasonably normal macroscopic and microscopic pattern, except for the marked thickening of its capsule. This differs from Turunen's[8] observation that the spleen became atrophic and colorless in the 5 dogs which he observed for from 2 to 4½ months. This apparently was a gross observation, as microscopic studies were not described. A possible explanation for the variation in results may be the fact that Turunen ligated the splenic vein at the level of the splenic hilum. In contradistinction to the method of splenic vein ligation used in the present study, ligation at the level of the hilum would be more likely to produce infarction of the spleen. Hoffman and Freedlander did not comment on the gross and microscopic status of the thoracic spleen in their report. Turunen also stated that venous collaterals between the spleen and lung were encountered but did not elaborate on this. In this study such channels have not yet been demonstrated. If anastomoses develop between the spleen and the pulmonary veins this could be a serious disadvantage. It would allow shunting of unoxygenated blood into the arterial circulation. There has been no evidence to date that this does happen but further observations are being made in the long-term survivors.

The experimental observations made to date indicate that thoracic transposition of the spleen is an effective method of decompression of an obstructed portal system. The procedure results in prompt formation of extensive splenothoracic collaterals. This collateral formation is a progressive phenomenon, the duration of which has not yet been determined. The most striking evidence of the efficacy of transposition of the spleen as a method of decompressing an obstructed portal venous system was obtained in the dogs which tolerated acute ligation of the portal vein. Such a ligation is uniformly fatal in the normal dog[1-4] but 73 per cent of animals with thoracic splenic transposi-

Fig. 11. Portogram in a Group V animal taken 1 week after acute ligation of the common portal vein.

Fig. 12. Splenogram which illustrates the prominent role of intercostal veins in the splenothoracic venous anastomoses after thoracic transposition of the spleen (Group II animal 2 months after transposition).

Fig. 13. Splenogram which illustrates unidentified veins connecting the splenic venous system and the azygos vein. Note right atrial filling. Other observations would indicate that the inferior caval filling is via phrenic veins.

tion survived acute interruption of the portal vein in this study. This is a larger percentage of survivors than was obtained by Hoffman and Freedlander in their study, but it should be noted that these authors did not attempt to stimulate splenothoracic collaterals by increasing the pressure in the portal or splenic venous systems.[4]

The final objective of this study was to gain information regarding the nature and extent of splenothoracic venous collaterals. It is important to note that these collaterals could be demonstrated readily by either portography or splenography, thus indicating free communication between these systems. The major collateral channels connected the spleen and the azygos system of veins. The intercostal veins played a major role in this communication. However, the phrenic, pericardiophrenic, and internal mammary veins also entered into venous anastomoses with the spleen. These latter veins were particularly prominent in instances in which the spleen was placed against the mediastinum rather than the posterolateral chest wall. In addition to the venous collaterals mentioned, splenography repeatedly demonstrated many large, unidentifiable splenothoracic venous channels. These probably represented small pleural veins which became enlarged. The propensity of the spleen to develop very large and bizarre venous collaterals was emphasized by the findings in the animals of Group III. In these animals after the spleen had been mobilized so that only the vein and artery constituted the splenic pedicle, the spleen was returned to the abdomen. One week later the splenic vein was ligated in such a manner that the communication between the splenic and gastric veins was preserved. In all of these animals very large networks of venous channels developed in the splenic hilum.

The phenomenon of autoplastic transplantation of splenic tissue (splenosis) after traumatic rupture of the spleen has long been known.[2] Splenic tissue can be readily transplanted into all the serous cavities of dogs, rabbits, and rats. It can also be transplanted subcutaneously or into the liver. These transplants usually have the appearance of normal splenic tissue and there is a striking absence of inflammatory reaction in the adjacent tissues. The implants usually develop a demonstrable artery and vein. These propensities of splenic tissue may be related to the manner in which a thoracic spleen promptly develops venous anastomotic communications.

Many questions concerning thoracic transposition of the spleen remain unanswered. The exact site of the anastomotic connections is not certain. The studies to date indicate that the splenic hilum and the diaphragm are a major site of collateral formation. However, there is also evidence that such channels develop between the splenic capsule and the various thoracic structures. More exact definition must await further investigation by careful anatomic dissection and corrosion studies. The questions concerning splenopulmonary venous communications and of the bacteriologic status of the

splenic pulp have already been mentioned.

The experimental results obtained to date would seem to indicate that thoracic transposition of the spleen is both a safe and effective method of decompressing an obstructed portal venous system, and that the procedure warrants adequate clinical trial. The procedure seems particularly well adapted to the patient with portal hypertension and hemorrhage from esophageal varices in whom a portal-systemic venous shunt is not feasible or possible. Patients in whom a portocaval shunt carries an excessively high risk and patients with an extrahepatic thrombosis of the portal vein might be logical candidates for this procedure. The influence of thoracic transposition of the spleen on ascites associated with portal hypertension is totally uncertain. Theoretically the procedure might have the same effect as a side-to-side portocaval shunt. Further experimental and clinical studies are clearly needed.

SUMMARY

An experimental evaluation of thoracic transposition of the spleen as a method of decompressing an obstructed portal system has been conducted.

The spleen was transposed into the left pleural cavity in 48 dogs. Survivors have now been followed for from 3 to 11 months and have remained in good health with no evidence of deleterious effects as a result of the procedure.

Splenography was used to demonstrate the prompt development of extensive splenothoracic venous anastomoses.

Whereas in the normal dog acute ligation of the portal vein is uniformly fatal, 73 per cent of the dogs with thoracic transposition of the spleen survived acute ligation of the portal vein.

The nature and extent of splenothoracic venous collaterals were described and discussed.

The results indicate that the procedure is a relatively safe and effective method of decompressing the portal system and suggest that adequate clinical trial is warranted.

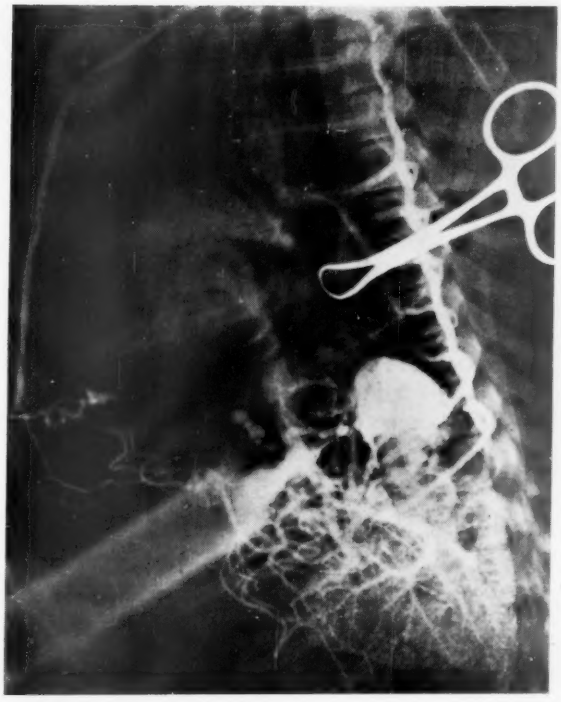

Fig. 14. Splenogram which shows filling of internal mammary vein as well as the azygos system in a Group II animal. Thoracic inferior vena cava again is visualized.

Fig. 15. Splenogram which demonstrates phrenic vein draining directly into the thoracic inferior vena cava.

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DISCUSSION

Dr. Robert R. Linton. I would like to question the advisability of this type of procedure for patients with portal hypertension. I must say that my tongue was hanging out a little when Dr. Scott showed us the mobilized large spleen, and yet he didn't take it out and perform a splenorenal shunt in their one temporarily successful case.

It has been my experience that in this type of case it is not too difficult to create a satisfactory end-to-side splenorenal shunt. We have demonstrated that, in those in whom this is possible, the patients have done extraordinarily well in the majority of cases. Our impression at the present time is that the patients with splenorenal shunts recover better than those with direct portacaval shunts. We are attempting at this time to get a follow-up on all the splenorenal and portacaval shunts that we have performed during the past 15 years to determine, if possible from this analysis, which is the better procedure.

This is an interesting approach to the problem, but I doubt that the procedure will be one which will replace shunt surgery.

Dr. John H. Foster. In response to Dr. Linton's comments, there are two points worthy of emphasis. First, most reported series of splenorenal shunts have shown a very high incidence of thrombosis and recurrence of esophageal hemorrhage, in the range of 20 to 30 per cent. This is in accord with our limited experience. I believe it is fair to say that Dr. Linton is in the minority when he states that the splenorenal shunt is preferable to the direct portacaval shunt in the treatment of portal hypertension.

Second, there are certainly instances when neither a splenorenal shunt nor a direct portacaval shunt is possible. It is in such cases that we believe thoracic transposition of the spleen deserves clinical trial. We are by no means advocating this procedure in all cases of portal hypertension.

Renal effects of temporary extensive infrarenal arterial occlusion: an experimental study

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Acute renal insufficiency is an occasional complication after reconstructive vascular procedures in which the aorta has been cross-clamped below the renal arteries. Of 475 arterial reconstructive operations at the University of California Hospital which required cross-clamping of the infrarenal abdominal aorta, postoperative renal failure was the cause of death in 7 cases. In 4 patients renal failure was explainable on the basis of shock, blood loss, or renal artery occlusion. In the remaining 3 patients no explanation was evident for the development of postoperative renal failure. Powers, Boba, and Stein[4] have reported that during a 12-month period at the Albany Hospital, 20 per cent of patients who had undergone abdominal aortic aneurysmectomy developed azotemia postoperatively.

In the same article Powers and his coworkers reported a study on 5 dogs in which renal blood flow had decreased significantly during temporary infrarenal aortic occlusion. Postoperatively the dogs developed acute tubular necrosis. These investigators also reported, as a result of subsequent experiments, that this complication could be prevented by denervation of the kidney or by the systemic administration of the ganglionic blocking agent Arfonad. Nanson and Noble[3] also reported the consistent occurrence of renal tubular necrosis in dogs after 2 hours of aortic cross-clamping below the renal arteries. They were able to prevent this by infiltration of the renal pedicle with Xylocaine during occlusion.

During the time that the description of our experiment was being prepared for publication, Gagnon, Bolt, Clarke, and Geever[1] published an article which reported their inability to cause renal insufficiency by occlusion of the infrarenal aorta. Para-aminohippuric acid clearance studies showed that only a transient decrease in renal blood flow had occurred during the occlusion period.

The results of our studies confirmed those of Gagnon and his co-workers and offer further evidence that temporary extensive infrarenal arterial occlusion is probably not a direct cause of postoperative renal insufficiency.

METHODS

The experiments to be described were conducted on 90 normal mongrel dogs. The animals were anesthetized with intravenously administered Nembutal. During the entire operative procedure the mean arterial blood pressure was monitored by means of a mercury manometer attached to a cannula within the carotid artery. Tests of renal function were made both preoperatively and postoperatively. These tests included measurement of serum creatinine, nonprotein nitrogen, and excretion of phenolsulfon-

Supported by a grant from the Sonoma County Heart Association.

Read at the Fourteenth Annual Meeting of the Society for Vascular Surgery, Miami Beach, Fla., June 12, 1960.

Table I. *Temporary aortic occlusion at level A (trifurcation)*

	No. animals	*Hours occluded*
Systemic heparinization		
	2	2
	2	3
	2	4
No heparin		
	2	2
	2	3
	3	4
Total	13	

All animals received operative hydration.

Table II. *Temporary aortic occlusion at level B (0.5 cm. distal to renal arteries)*

	No. animals	*Hours occluded*
Operative hydration		
	3	2
	3	3
	2	4
No operative hydration		
	3	3
	7	6
Preoperative dehydration		
	3	3
Total	21	

Table III

	No. animals	*Hours occluded*
Simultaneous vena cava occlusion and operative hydration		
	2	2
	3	3
	3	4
Previous unilateral nephrectomy without operative hydration		
	3	3
	4*	6
	3	6
Total	18	

*Systemic heparinization.

phthalein. A specimen of renal tissue was obtained at operation and at necropsy. All of the surviving animals were maintained in a metabolism cage for 6 to 7 days postoperatively and then were sacrificed. Pertinent observations during this period, in addition to the renal function tests already mentioned, included daily measurements of fluid intake, urinary output, and the changes in weight of each animal.

The first portion of this study included experiments in which the effects of a single aortic occlusion were observed. In the first series of these experiments, in a group of 13 animals, the aorta was occluded approximately 1 cm. above the trifurcation for periods of between 2 and 4 hours (Table I). Six animals in this group were systemically heparinized (1.5 mg. per kilogram) during the period of aortic occlusion.

To explore the possible associated effects of operative dissection in the area of the renal pedicle, we performed 21 experiments in which the aorta was occluded approximately 0.5 cm. distal to the renal arteries for periods ranging from 2 to 6 hours (Table II). Varying degrees of dehydration were produced by withholding fluids during operation in 10 animals and for 48 hours prior to operation in 3 animals.

In a third group of experiments the effects of sudden massive release of blood from partially ischemic tissues were studied by means of simultaneous cross-clamping of the inferior vena cava during periods of aortic occlusion in 8 animals (Table III). Occlusion times of both aorta and inferior vena cava varied from 2 to 4 hours.

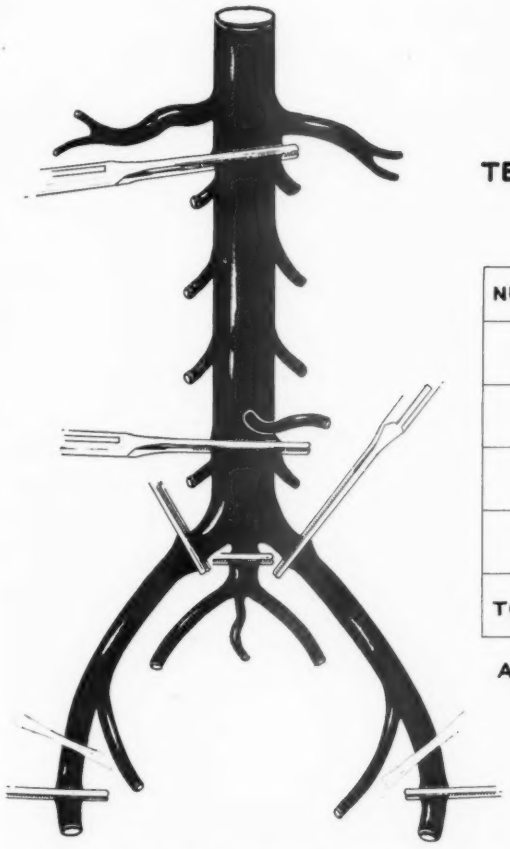
In 10 animals unilateral nephrectomy had been performed 1 week prior to the aortic cross-clamping experiment to determine the effect of aortic occlusion when renal mass was reduced. Periods of occlusion were maintained between 3 and 6 hours in this group. In the foregoing experiments, pressure determinations in the arterial tree distal to the level of aortic occlusion showed average pressures of 50 mm. Hg. To study the effect on renal function of the release of blood from more ischemic tissue than had been

produced by single aortic occlusion, multiple cross-clamping of the distal arterial tree was performed in 20 animals (Fig. 1). Distal arterial pressure was thereby reduced to approximately 10 mm. Hg. Systemic heparinization was maintained for periods of occlusion varying from 3 to 6 hours. Ten of 11 animals in which occlusion was maintained for 6 hours died within 24 hours, during which time the reduction in blood pressure had become progressively more severe. The cause of death in the 10 animals appeared to be unrelated to alteration in renal function and is currently the subject of a further study.

In 4 animals, unilateral renal blood flow was measured continuously before, during, and after a single infrarenal aortic occlusion by means of an electromagnetic flowmeter with the flowmeter probe placed around the right renal artery.[2] The occlusive period was 2 hours in this group.

RESULTS

Eighty-six normal mongrel dogs were used in the course of this study. Twenty-four animals died prior to completion of the observation period from causes unrelated to renal insufficiency. These animals are not included in this report, which is, therefore, based on observations made on the remaining 62 animals. Sixty animals showed no alteration in renal function or morphologic condition as a result of infrarenal aortic and arterial occlusion with the variables described in this study. In 4 additional dogs, in which renal blood flow was observed with an electromagnetic flowmeter at the time of infrarenal aortic occlusion, no changes in mean blood flow occurred during or after occlusion (Fig. 2). Only 2 dogs showed histologic evidence of renal damage. One of these animals showed decreased renal function and developed azotemia postoperatively.



TEMPORARY MULTIPLE ARTERIAL OCCLUSION

NUMBER OF ANIMALS	HOURS OCCLUDED
1	3
6	4
2	5
11	6
TOTAL 20	

ALL ANIMALS RECEIVED OPERATIVE HYDRATION AND SYSTEMIC HEPARINIZATION

Fig. 1. Sites and duration of arterial occlusion in multiple occlusion experiment.

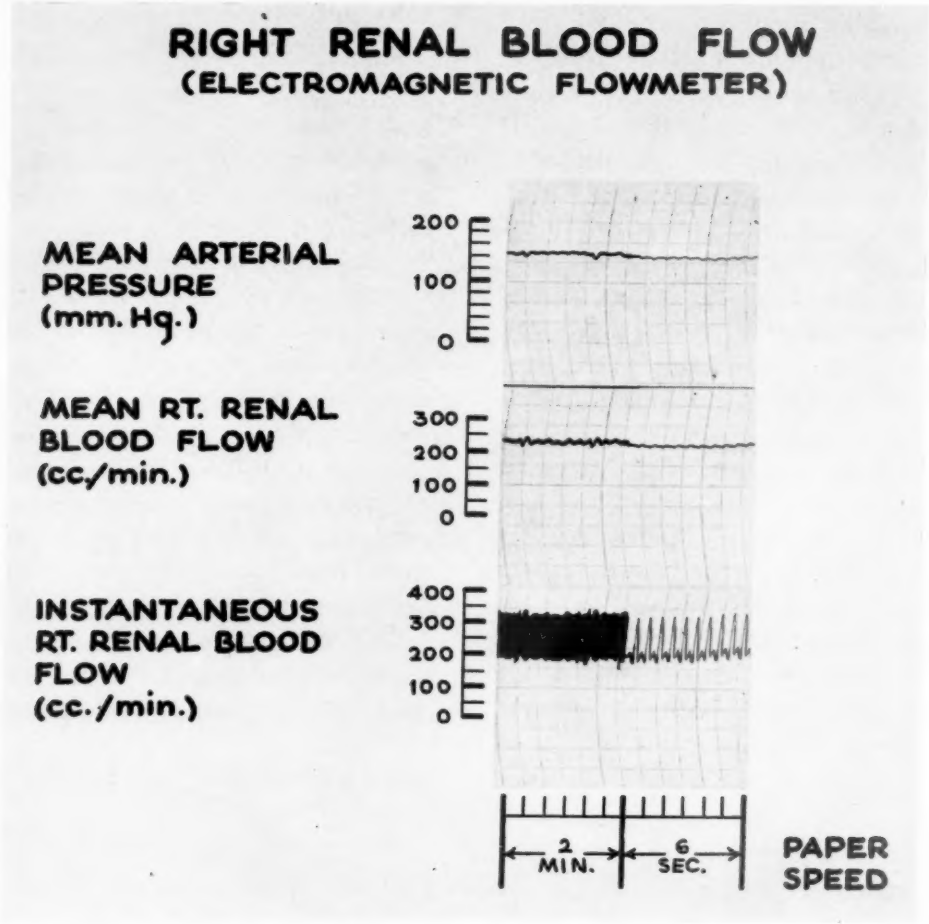


Fig. 2, A. Polygraph tracings which were made while electromagnetic flowmeter probe was applied to the right renal artery in a control animal.

This was the only animal in the entire series in which postoperative decrease in renal function became apparent.

The animal that showed postoperative decrease in renal function and tubular necrosis at necropsy was one of 4 which had had a previous nephrectomy and which had been subjected to 6 hours of aortic occlusion 0.5 cm. distal to the renal arteries with systemic heparinization (Fig. 3). In the remaining 3 dogs in this group, as well as in 3 additional unheparinized dogs that had undergone a previous unilateral nephrectomy and 6 hours of occlusion, no disturbances in renal function or morphologic condition were observed.

In the second dog which showed renal damage, multiple vascular occlusions had been maintained for a period of 4 hours. In this animal the results of renal function tests remained normal postoperatively, although infarction necrosis was actually found upon examination of a section of renal tissue obtained at necropsy 1 week after the operative procedure. This suggests that focal renal infarction had occurred, as evidenced by the results of the postmortem examination of the kidney, but the amount of renal tissue involved was not sufficient to alter renal function. If renal damage occurs as a direct result of prolonged cross-clamping of the infrarenal aorta, it would be expected to involve the kidney diffusely. Consequently the results obtained in the animal described support the concept that the observed renal pathologic changes are attributable to causes other than the cross-clamping itself.

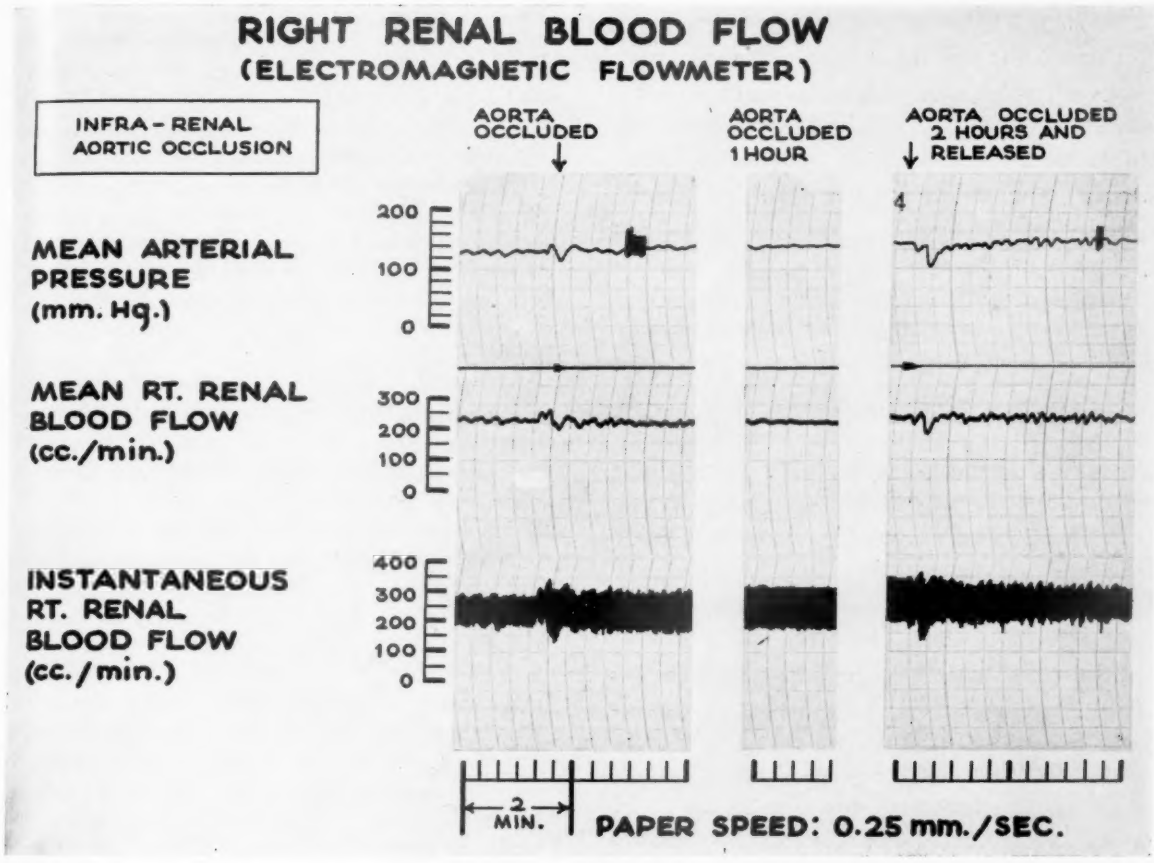


Fig. 2, B. Renal arterial blood flow (electromagnetic flowmeter) and arterial pressure observations made during a 2-hour period of infrarenal aortic occlusion. Note momentary variation in renal blood flow at time of application and release of arotic clamp which parallels the alteration in systemic blood pressure.

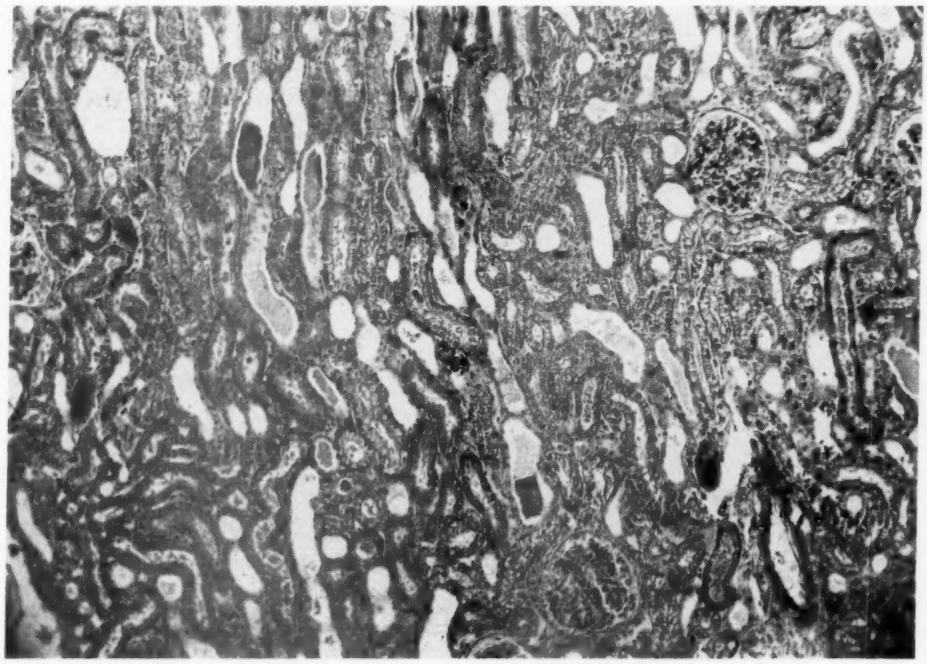


Fig. 3. Histologic section which demonstrates tubular necrosis in the one animal in which postoperative renal insufficiency occurred.

SUMMARY

The effects on the kidney of temporary extensive infrarenal arterial occlusion were studied in 66 dogs. Variables introduced into this experiment included systemic heparinization, alterations in the level and multiplicity of arterial occlusion, simultaneous occlusion of the inferior vena cava, the degree of hydration of the animal at the time of occlusion, and reduction in renal mass prior to occlusion. Renal blood flow was measured continuously before, during, and after a single 2-hour infrarenal aortic occlusion by means of an electromagnetic flowmeter applied to the renal artery.

Sixty-one dogs showed unaltered renal function and no evidence of tubular necrosis. Only 1 dog in the entire study showed changes compatible with tubular necrosis. In the only 4 animals in which the mean renal blood flow was measured, no significant changes occurred. As a result it may be inferred that temporary extensive infrarenal arterial occlusion is not a direct cause of postoperative renal insufficiency.

We are grateful to Mr. Burt B. Rutkin for the development and calibration of the electromagnetic flowmeter used in these experiments.

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DISCUSSION

Dr. Samuel R. Powers, Jr. I think that this is an interesting paper which helps considerably to assess the severity of the insult which results from cross-clamping of the infrarenal aorta. It is important to realize that the rigidly controlled experimental conditions are not quite analogous to the clinical situation during resection of an abdominal aneurysm or to the experimental situation in our studies. The addition of considerable operative trauma and frequently considerable blood loss are unquestionably important factors in the production of tubular necrosis. We all seem to agree that cross-clamping the aorta will produce a decrease in renal blood flow, especially when the direct method is used, and even some definite but readily reversible histologic changes in the kidney. These changes are temporary unless the additional factor of shock or even moderate hypotension develops, as it must have in the one experiment shown today. Cross-clamping the aorta can, therefore, be considered as one of the factors which will adversely affect renal function. We believe that this effect is preventable and when prevented should result in a lower incidence of renal shutdown.

Dr. John H. Foster. I should like to congratulate Dr. McGonigle and his associates on a very fine experimental study. At Vanderbilt we, too, have been interested in the influence on the kidneys of lower abdominal aortic cross-clamping and a brief résumé of a study we have just completed may be of interest. In a control group of 10 dogs the aorta was occluded immediately below the renal arteries for 2 hours. Postoperative studies of the serum nonprotein nitrogen in the ensuing week revealed normal values. Renal biopsies at the end of 1 week showed an absence of significant change in comparison with preocclusion biopsies. In a second group of 6 animals, renal blood flow was measured directly during the 2-hour period of aortic occlusion. We used a previously described direct method of measuring renal blood flow, a method which avoids trauma to the renal veins. Biopsy studies and serum nonprotein nitrogen determinations in these animals yielded the same results as obtained in the control group. During the period of aortic occlusion the renal blood flow characteristically decreased 15 to 20 per cent in each animal, but in the follow-up period renal function remained normal and tubular necrosis did not occur. Our results place us in agreement with Dr. McGonigle. Infrarenal aortic occlusion in the dog did not produce significant renal tubular damage. Under the conditions of the study a consistent but moderate decrease in renal blood flow did occur.

Dr. Edwin J. Wylie. Our original purpose in undertaking this study was to attempt to define more fully the nature of the mechanism responsible for the presumed reduction of renal blood flow after cross-clamping of the infrarenal abdominal aorta. Although results obtained from experiments conducted at Walter Reed Hospital have indicated that significant reduction of renal blood flow does not occur under these circumstances, this information was not published until

quite recently. Our studies also seem to indicate that under the conditions of this experiment, renal blood flow does not decrease. It is significant that as experience in abdominal aortic surgery increases, the complication of postoperative renal depression has almost disappeared.

It is quite possible that in performing these studies we have overlooked an unknown factor that has contributed to the development of renal damage in clinical experience. I am prompted to make this comment by 2 instances of fatal renal damage that we have observed under seemingly benign conditions. The first developed after an uneventful thromboendarterectomy of the common iliac artery in a 45-year-old man who, because of the suddenness of the occlusion, had developed severe ischemic changes in the involved leg. Although an uneventful operation returned total flow to the leg, permanent cessation of renal function developed.

The second experience occurred after an uneventful popliteal embolectomy, a 1-hour operation performed under low unilateral spinal anesthesia. Return of blood supply to the lower leg was complete. The calf rapidly became hot and swollen. Pulses were bounding. Without apparent cause, renal function abruptly and permanently ceased. Pathologic studies in both cases showed acute tubular necrosis without evidence of vascular occlusion.

Inasmuch as we have failed to demonstrate experimentally either decreased renal blood flow or renal damage in analogous situations whereby normal blood flow is restored to severely ischemic tissue, the cause of this rare complication remains obscure.

Dr. Dee J. McGonigle, Jr. We wish to express our appreciation to each of the discussants for his comments concerning our paper. It is quite interesting to learn of your experiences in this area.

Arterioplasty for severe ischemia of the lower limbs: indications and results

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We have long shared the widely held opinion that the management by reconstructive surgical procedures of the advanced forms of peripheral arterial insufficiency (characterized by severe rest pain, pregangrene, or localized early gangrene, or a combination of these manifestations), in general, presents particularly difficult problems of case selection. In order to better define the clinical and angiographic criteria that have bearing on the success rate of angioplastic operations in this category of lesions and, thus, to establish a firmer basis for the choice of surgical procedures in their treatment, we have reviewed the histories of a group of consecutive patients whose clinical complaint involved one or more of the manifestations of severe ischemia at rest and who were treated with reconstructive surgical procedures, principally grafting.

CLINICAL MATERIAL

The survey comprised 130 angioplastic operations performed on 108 patients with severe ischemia of the lower limbs (Table I). Patients whose principal complaint was intermittent claudication were not included even though some rest pain of mild degree may have been a part of the clinical picture. The degree of ischemia regarded as the necessary criterion for inclusion in the study was that which, in addition to a marked impairment of walking ability, was characterized by pain at rest requiring medication and by local tissue changes of various severity such as dusky discoloration, dependent rubor, elevation pallor, atrophy of the skin and its appendages, and also atrophy of the musculature. We regard these changes as essentially pregangrenous. Once established, they will, on trivial trauma or as a result of a slight progression of the occlusive process, advance to irreversible, deep, unhealing gangrene of varying extent.

The ischemic manifestations enumerated can be placed in 3 groups of increasing severity, (1) severe rest pain and pregangrenous tissue changes, (2) severe rest pain and localized deep gangrene or skin ulceration, and (3) extensive deep gangrene. It is patients with the first two manifestations that formed the subjects of the study. The third manifestation is the result of occlusive involvement of the arterial system which is so advanced that surgical correction is not possible. The degree of discomfort or pain at rest was always severe enough to require medication, often medication of vigorous character. The pregangrenous tissue changes included all the degrees of ischemia up to the limit of irreversible tissue death. Deep gangrene was defined as localized if it involved only the toes. Skin ulceration, always initiated by trauma which was usually of trivial character, was regarded as ischemic only if the indolence was entirely or mainly due to lack of blood supply. Skin defects of slow healing that were primarily stasic were excluded.

Read at the Fourteenth Annual Meeting of the Society for Vascular Surgery, Miami Beach, Fla., June 12, 1960.

Separate consideration must be given to the definition of a small but very important clinical group of patients, the group whose ischemic manifestations are of abrupt onset. The pathologic physiology of these patients will be discussed presently. At this point it is to be stated that while in general these patients fit well into the group with rest pain without gangrene, at times, when appropriate treatment is delayed or omitted, they proceed on a rapid course leading to extensive deep gangrene.

Mode of follow-up. All the patients were continuously observed at clinic visits 2 weeks to 12 months apart. All were studied by means of angiograms both before and after operation. Whenever possible the following routine was maintained: first postoperative visit at 4 weeks, first postoperative angiogram at 6 weeks, subsequent clinical visit at 6 to 12 months, and subsequent angiographic checks at 12 months. At times conditions of diverse nature caused modification of this routine, and the time intervals were shortened or lengthened. No patient was lost from observation, and all were seen within 3 months of the closing date of this survey (May 31, 1960). The lengths of follow-up periods were tabulated as of the date of the last clinic visit.

Considerations of morbid physiology. The pathologic circumstances that result in severe rest ischemia have 3 aspects, the aspect of spatial extent of the lesions, the aspect of temporal relations of the occlusive process, and the aspect of the anatomic features of the segment or segments of the affected arterial tree.

A single occlusive lesion probably never results in severe rest ischemia. If it seems to do so the information (which, obviously, is always angiographic) on which the diagnosis of the singularity of the lesion is based is probably incomplete or misleading. Localized segmental occlusion in the presence of a patent proximal and distal arterial tree almost always affords the opportunity for the development of a collateral circulation of sufficient amplitude to provide to the distal part a blood flow that is adequate for the needs of the tissues at rest. The only exception to this rule is the type of sudden segmental occlusion in which, because of neglect or other factors, distal clotting takes place. Under these conditions, however, one cannot rightfully speak of a single occlusive lesion.

When multiple occlusive lesions are present, on the other hand, the development of the collateral circulation is progressively more and more deficient distally. Because the dilatation of the resting collateral arteries is entirely dependent on pressure relationships, as the arterial pressure drops at the site of the proximal point of occlusion, the pressure available for the filling of the next distal collateral bed becomes less. This summation of the decrease in blood pressure and, consequently, volume flow, readily leads to the degree of ischemia that will be symptomatic even at rest. In our survey every patient with two completely occluding lesions in anatomic sequence, regardless of the regional localization, suffered from ischemia in this range of magnitude. In terms of finer grading of the severity of ischemia, there are, of course, variations. In this respect, the recognition of the anatomic subdivision of the distal arterial tree into functional segments, the contemporaneous obliteration of any one of which leads to severe ischemia, has practical importance. The subdivisions are the common iliac, the external iliac—common femoral, the superficial femoral, the popliteal (distal from

Table I. *Clinical material (130 lesions with rest ischemia)*

Degree of disease	*Aortoiliac*	*Femoropopliteal*	*Combined*	*Total*
Rest pain	14	33	26	73 (56%)
Rest pain and gangrene	3	30	24	57 (44%)
Totals	17 (13%)	63 (49%)	50 (38%)	130

the superior genicular branches), the anterior tibial, the posterior tibial, and the peroneal. The most commonly seen combination is a segmental occlusion of the superficial femoral artery and one or more of the branches of the popliteal artery. When this type of lesion is associated with an occlusion on the iliac level, the most severe degree of ischemia results.

With regard to the temporal relations of the occlusive process,* the intimal changes leading to stenosis are probably always very slowly progressive. In over 80 per cent of the cases stenosis reaches a high grade and remains in this state without complete occlusion by thrombosis for a very long period of time, probably for many months (Table II). During this time the potential collateral bed can dilate to its fullest. In a small proportion of the cases, however, for reasons which we do not understand, the thrombosis (which always constitutes the terminal event) occurs while the intimal thickening is only slightly advanced and 30 per cent or more of the arterial lumen is still open. At the early stage of stenosis the development of the collateral bed is still rudimentary or even absent, and the sudden completion of the obliteration of the lumen leads to a severe decrease of blood flow distal to the occlusion. If the occlusive lesion is single, the potential collateral pathways are still adequate to provide the small volume flow of blood essential for the survival of the tissues at rest. With time the collateral branches dilate and satisfactory compensation may take place, leaving perhaps some degree of ischemia on exercise (intermittent claudication) as a residual effect. If, however, a second distal or proximal occlusive lesion is present, or (which ultimately amounts to the same) a distal thrombotic complication ensues, the emergency compensatory mechanism may be inadequate and tissue death will take place.

*In the discussion, sudden arterial occlusion is always assumed to refer to thrombotic obliteration. Occlusion by embolization, which as a rule can be readily differentiated, does not form the subject of the remarks.

Table II. *Incidence of sudden and insidious development in rest ischemia*

Location of main lesion	*Sudden onset*	*Insidious onset*
Aortoiliac	4 (23%)	13
Femoropopliteal	11 (17%)	52
Combined	12 (24%)	38
Total 130	27 (21%)	103

It is hardly necessary to point out that the anatomic characteristics of the arterial segment or segments involved in the occlusive process have serious bearing on the severity of manifestations under all circumstances. In the aortoiliac and femoral regions, as far distally as the superior genicular arteries, the potential collateral beds available for the establishment of compensatory circulation are ample. From the superior genicular branches of the femoral artery to the inferior genicular branches of the popliteal artery the anastomotic communications are only fair, and distal from the latter artery they are meager. For this reason the consequences of the occlusion of the popliteal arterial branches are more serious than those of similar lesions, whether single or multiple, which are further proximal.

The considerations of anatomy and physiology enumerated are, of course, of great practical importance in the therapeutic approach to severe rest ischemia.

PRINCIPLES OF MANAGEMENT

The survey spans a period of 8 years. During this time a number of changes have taken place in the general field of vascular surgery with regard to both principles and practice, and our approach to the problems of the surgical treatment of rest ischemia has reflected these changes. It would be without advantage to recount these variations of method, now only of historical interest. In the following description, only procedures currently used will be presented.

The principles of action appropriate for the treatment of the 2 types of clinical manifestations (that is, ischemia of sudden

onset and ischemia of insidious development) are basically different.

Peripheral ischemia caused by occlusive arterial disease of *sudden onset* is regarded as a clinical situation of urgent and often emergent character. As described before, the physiologic and anatomic characteristics of the occlusive lesion strongly favor the establishment of a compensatory mechanism that prevents tissue death in the large majority of cases. Nevertheless, in 10 to 20 per cent of the instances the ischemia will result in gangrene unless the obstruction is relieved. This threat demands the most attentive observation of the affected limb lest intervention be delayed too long or carried out at an inappropriate time. An attempt at immediate operative correction of all such lesions has been found to be an unsatisfactory routine for several reasons. First, adequate angiographic visualization of the occlusive arterial lesion immediately after the acute onset, without which a rational plan of operation is difficult to formulate, carries an increased risk. Second, the success of the corrective surgical procedure is diminished by the absence of collateral arterial pathways at this stage. Third, the patient in the midst of the vascular accident is not an ideal subject for a major surgical intervention. It is much more desirable to limit the immediate surgical intervention to those cases in which the compensatory arterial mechanism is inadequate and gangrene threatens. During the period of observation, the interruption of the lumbar sympathetic chain by local anesthetic agents is very useful. The administration of 5 to 8 ml. of 0.5 per cent Nesacaine solution every 3 to 4 hours through an inlying epidural catheter for up to 72 hours has been a satisfactory clinical method. Once the threat of tissue death has passed, a period of 3 to 7 days is allowed for the collateral arterial compensation to become well established, and then the occlusive process is investigated with angiography. If the arterial pattern permits of angioplastic correction, the appropriate surgical procedure is performed. The residual disability from ischemia brought on by sudden thrombotic occlusion is usually so severe that surgical treatment, if at all possible, is mandatory.

If, after the sudden onset of thrombosis, the ischemia of the limb fails to improve to the degree that is necessary for tissue viability in spite of auxiliary measures, operative treatment is undertaken. The precise assessment of the evolution of the ischemic changes in the limb is one of the most difficult tasks in the difficult art of the exercise of clinical judgment. We have found that as long as the motor function of the small muscles of the foot is present, the degree of ischemia has not yet reached the stage at which tissue death threatens. In planning the surgical procedure immediately after the acute onset, the use of preoperative angiography is avoided. If unavoidable, angiography is performed intraoperatively.

In cases of ischemia of *insidious development* there is no therapeutic urgency and a planned routine is followed. This routine includes, besides the assessment of the total patient for operative risk, the careful roentgen visualization of the abdominal aorta and its peripheral branches as far distally as the divisions of the popliteal artery.

Technical considerations. In keeping with the general trend in peripheral vascular surgery, the most commonly used angioplastic technique in the treatment of these patients was bypass grafting. Indeed, in occlusive arterial disease of the state of advancement that characterizes rest ischemia, thromboendarterectomy as the principal technical method has been found inapplicable. It is important to stress that, besides other advantages, bypass grafting allows the least possible interference with the functioning collateral circulation, which in advanced occlusive arteriopathy is of the utmost importance.

In the application of the bypass technique an attitude has been adopted which, upon the whole, is one of conservatism compatible with adequate correction of the occlusive lesion. In the aortoiliac area, in incomplete iliac lesions, the intervention is limited to

the side with complete occlusion and the diseased but unoccluded side is left intact. In combined lesions with complete aortoiliac and femoropopliteal occlusion only the proximal lesion is, as a rule, corrected. In femoropopliteal lesions the entire femoropopliteal trunk is bypassed. In the latter anatomic region the principle of conservatism is perhaps violated, since an attempt is made for the correction of even very advanced lesions. Indeed, correction is tried as long as an open popliteal stem with at least one open major division is present.

The role of sympathectomy. Unless deep gangrene involving the dorsum or the sole of the foot is present, when reconstructive surgical treatment is not possible, amputation is not recommended for rest ischemia until a lumbar sympathectomy has been tried. An analysis of the result of this operation is not the subject of this study but it can be said that in 20 to 30 per cent of the cases, worthwhile prolongation of the life of the limb can be achieved.

RESULTS

Even a brief review of the tables listing the results of this study readily shows that only slightly over 10 per cent of the patients have been observed for more than 2 years. This would seem to be a statistical deficiency that may raise serious doubt concerning the justification for the presentation of these figures. Further reflection, however, dispels this doubt, at least in part.

Until about 2 years ago we used angioplastic operations only sparingly in the treatment of rest ischemia. In the early phase of our experience with reconstructive vascular operations for this disease, the immediate failure rate as compared with that of the treatment of intermittent claudication seemed prohibitively high. About 3 years ago, the continued follow-up observation of the postoperative course of patients with occlusive arteriopathy began to reveal 2 significant facts. First, the late results of the operations for intermittent claudication caused by femoral lesions deteriorated much more rapidly than we had anticipated (further discussion of this finding is not pertinent at this time). Second, the results of the operations for rest ischemia that did not fail immediately or soon after the operation showed a late patency rate that was not markedly different from that seen after operations for intermittent claudication. Since there was good reason to hope that the immediate and early postoperative results could also be improved, thanks to the newer technical methods of grafting, we turned to a wider use of grafting procedures in the treatment of rest ischemia. The present survey was undertaken primarily to assess these early results, or the first 2 years of the wider application of reconstructive techniques.

The results of this experience are listed according to the anatomic location of the main obstructing lesions in Table III and according to the severity of disease in Tables IV and V. (It should be clearly kept in mind that the data in Tables III, IV, V, and VI are not cumulative.) Both the immediate and early results are satisfactory. The much smaller group of patients with follow-up for from 2 to 7 years suggest that these results may well persist. It should be stressed, moreover, that when dealing with the type of advanced occlusive disease we are discussing, one's criteria of satisfactory late results ought to be more modest than when dealing with less severe disease such as that concerned with intermittent claudication. If a severely ischemic limb can be restored by a grafting procedure to a normal functional state or at least to a state of comfort and minimal function compatible with useful life for 2 years, the results would seem to be fully commensurate with risk and cost of the operation. The results so far obtained give promise of the achievement of this minimal goal in approximately two-thirds of the patients treated.

An impression of the value of the surgical treatment of rest ischemia can be gained also from the consideration of the amputation rate listed in Table VI. In this respect, certain standards of judgment must be first clarified. Among the patients with severe rest pain but no gangrene, undoubtedly

Table III. *Results of angioplasty for rest ischemia according to location of main lesion*

Location of lesion and no. of operations	*Immediate (1-30 days)*		*Early (1-24 mo.)*		*Late (2-7 yr.)*	
	Open	*Closed*	*Open*	*Closed*	*Open*	*Closed*
Aortoiliac (17)	15 (88%)	2	13 (87%)	2	1	0
Femoropopliteal (63)	44 (70%)	19	29 (66%)	15	3 (75%)	1
Combined (50)	39 (78%)	11	33 (84%)	6	11	0

Table IV. *Results of angioplasty for occlusive disease of various severity (aortoiliac operations)*

Type of disease and no. of operations	*Immediate*		*Early (1-24 mo.)*		*Late (2-7 yr.)*	
	Open	*Closed*	*Open*	*Closed*	*Open*	*Closed*
Intermittent claudication (168)	147 (87%)	21	126 (86%)	21	66 (96%)	3
Rest pain (36)	30 (83%)	6	27 (90%)	3	8	0
Rest pain with gangrene (19)	17 (89%)	2	15 (79%)	4	3	0

Table V. *Results of angioplasty for occlusive disease of various severity (femoropopliteal operations)*

Type of disease and no. of operations	*Immediate*		*Early (1-24 mo.)*		*Late (2-7 yr.)*	
	Open	*Closed*	*Open*	*Closed*	*Open*	*Closed*
Intermittent claudication (160)	115 (72%)	45	68 (59%)	47	14 (61%)	9
Rest pain (38)	31 (81%)	7	20 (64%)	11	5	0
Rest pain with gangrene (35)	23 (66%)	12	16 (69%)	7	2	0

Table VI. *Postoperative incidence of amputations*

Type of disease	*No. of cases*	*Amputations*		*Postoperative time relation of amputations (%)*		
		No.	*%*	*0-2 mo.*	*3-12 mo.*	*13-60 mo.*
Rest pain	73	26	36	61	35	4
Rest pain and gangrene	57	25	44	72	20	8

there were some in which the unsuccessful angioplastic operation precipitated amputation, that is, in which the operation subtracted some months or perhaps years from the life of the limb. However, the loss was much less than the crude figures would suggest since the limbs were not only useless but a source of incapacitation and discomfort. On the other hand, there can be little doubt that in the group with rest pain and gangrene amputation was inevitable. In this group the limbs not amputated (56 per cent) were limbs saved. This impression is strengthened by the comparison of a group of patients with rest ischemia treated surgically with a group that for various reasons were not operated on and were continued under conservative management. The amputation rate in the latter group during a 6-year period of observation was almost twice the amputation rate observed in the surgically treated group.

In a discussion of results, a brief reference to 2 technical problems appears pertinent. When dealing with combined aortoiliac and femoropopliteal lesions with complete occlusion the surgeon has the option of correcting only the proximal lesion at the primary operation and leaving the distal lesion uncorrected (or if necessary subject it

Table VII. *Results in aortofemoral and aortopopliteal operations for combined lesions*

Type of operation	*Immediate*		*Early (1-12 mo.)*		*Early (13-24 mo.)*		*Late (2-7 yr.)*	
	Open	*Closed*	*Open*	*Closed*	*Open*	*Closed*	*Open*	*Closed*
Aortofemoral	7	2	5	0	18 (75%)	6	25 (71%)	10
Aortopopliteal	1	2	1	3	2	3	0	1

Table VIII. *Results in femorofemoral and femoropopliteal grafting (3-year follow-up)*

Type of operation	*Immediate*		*Cumulative late*	
	Open	*Closed*	*Open*	*Closed*
Femorofemoral	70 (71%)	29	28 (28%)	71
Femoropopliteal	62 (69%)	28	48 (53%)	42

to a second intervention), or of using a procedure that will relieve both obstructive lesions at once. The simpler operation is not only safer but, as shown in Table VII, yields superior results. The results listed in Table VIII clearly suggest that the so-called "long femoral" or "femoropopliteal" bypass yields better results than the "short femoral" or "femorofemoral" bypass formerly in vogue. This, of course, can be expected from the circumstance that the longer implant assures a more extensive bridging of the diseased or potentially diseased arterial trunk.

CONCLUSIONS

1. The use of grafting procedures in patients with severe ischemia of the lower limbs caused by occlusive arteriopathy is clearly indicated whenever the possibility of success exists and the patient's general condition permits the intervention.

2. The minimum technical requirement for femoropopliteal grafting in these cases is the presence of an open popliteal arterial stem with at least one functioning infrapopliteal branch. The minimum technical requirement for aortoiliac grafting is a functional common femoral arterial segment or the existence of an anatomic situation in the popliteal area described above.

3. A successful operation will always completely rehabilitate the patient. The duration of the rehabilitation is not known but it is probably at least 2 years in two-thirds of the cases. An unsuccessful operation may precipitate amputation but, under the operative indications described, such an amputation either is inevitable or merely means the loss of a functionless limb.

DISCUSSION

Dr. A. W. Humphries. I would like to express my appreciation for being permitted to hear Dr. Szilagyi's excellent paper on a subject which has been of great interest to me for a long period of time. I will take this opportunity to substantiate his figures by our own experience which parallels his and to perhaps express a more optimistic point of view as far as definitive treatment for these unfortunate people is concerned. We have had occasion to construct arterial grafts on 170 limbs followed for periods of up to 6 years in patients for whom operation was classified as nonelective, that is, those with severe rest pain, ulcer, or gangrene. I should like to make 3 points based upon the results we have obtained to date.

The over-all statistics at the present time on the 170 cases are: 90 of the initial grafts are open and the patients are symptom-free, 40 grafts were initially successful but shut down at a later date (however, 14 of the patients are clinically improved), 30 grafts were primary failures at the time of operation (3 of the patients strangely enough, are improved), and 10 patients died. In terms of percentage, there are 53 per cent graft successes but 63 per cent clinical successes. To us this is a worthwhile procedure for patients who are admitted either for amputation at the time or in the relatively near future.

One hundred and twenty-seven of the grafts were constructed once, 39 were attempted twice,

3 three times, and 1 four times. The percentages of success in the group that were operated on once are identical with the success percentages in the group who, having had grafting which failed, had regrafting. Therefore, if the graft was worth performing the first time, it is equally worthwhile to regraft at the time of late failure should late failure occur.

Finally, it is most interesting that 50 per cent of the late shutdowns had occurred by the end of the first year after the graft, 85 per cent by the end of the second year after the graft, and no late shutdowns have occurred after the third postoperative year. Therefore, in contrast to the initial disappointment of the relatively high shutdown rate, it should be borne in mind that the grafts which do stay open for 2 to 3 years are apt to continue to stay open.

There were 29 amputations in this group or 17 per cent of the total. Twenty-five of these occurred when grafts had been primary failures, in patients who were hopeless in the first place. Only 4 lost their legs at the time of the secondary or late occlusion of the graft.

Dr. Andrew Dale. There is increasingly widespread dissatisfaction with peripheral arterial grafting at the popliteal level and distal to that. Of course, the vessels are small and the technical performance of anastomosis is more difficult than in the larger proximal arteries. In addition to that problem, I believe that the commonly used synthetic tubes are particularly unsuitable for anastomosis to such small vessels for several reasons, which include development of a thick neointima at the anastomotic site as well as buckling of the plastic tube if it crosses a flexion crease.

I continue to believe that autogenous veins are superior materials for such distal small arterial anastomoses. It does appear, however, that various synthetic tubes are quite suitable for large arterial grafting.

In an effort to combine the advantages of synthetic tubes for larger proximal vessels and autogenous veins for small distal arteries, Dr. William Pridgen and I last summer began animal studies with composite grafts composed of a length of woven Teflon to which a segment of autogenous jugular vein was sutured by a special technique end-to-end. These were placed in dogs in the laboratory and appeared to function satisfactorily. Details will be reported later. Five such composite woven Teflon plus autogenous vein grafts have been placed in patients to date by Dr. Pridgen, Dr. John Foster, and I and early experience with these is satisfactory.

The first slide illustrates the technique of suturing the autogenous vein to the end of the synthetic tube. The second slide shows the composite graft in place in the femoral region of a dog. The third slide diagrammatically illustrates a long composite graft in a human patient, extending from external iliac artery to distal popliteal artery composed proximally of five-sixteenths inch crimped woven Teflon and distally of a 6 inch segment of autogenous saphenous vein. This was placed 4 months ago and successfully salvaged the extremity of a woman in whom one toe had begun to show pregangrenous brownish discoloration. It is to be emphasized that the follow-up on these composite grafts has been short, but it is thought that they may prove to be a useful modification of existing techniques.

Dr. Robert R. Linton. You have just heard a very excellent, honest, and clear-cut evaluation of angioplastic operations carried out by Dr. Szilagyi and his group.

Our experience with reconstructive arterial surgery using prostheses and arterial homografts has been so poor for lasting patency, despite a very high immediate success rate, that we do not use these except in very rare instances. At the present time I think I prefer the prosthesis to the homograft, but I am sure neither of these methods give nearly as good results as saphenous vein autografts or endarterectomy plus saphenous vein patch grafts, since with these one leaves the patient with all autogenous tissue for the arterial conduit that seems to remain patent for many years.

At the present time I also feel strongly that not only should one employ reconstructive arterial surgery for severe ischemia of the lower extremity in order to save a limb, but also use autogenous tissue as I have been doing to get excellent and long-lasting results in patients who are complaining only of intermittent claudication. My patients so treated certainly are some of the most grateful ones.

I disagree with many authorities in this field of reconstructive arterial surgery who hold that the cause of failure in many of the cases is the advance of the patient's disease. In my own patients it has been the failure of the grafts themselves (chiefly homografts or prostheses) in the great majority, and only rarely the advance of the atherosclerotic disease in the patient's arteries. My recommendation, therefore, is for more surgeons to utilize the venous autograft and/or the endarterectomy procedure.

Dr. John H. Olwin. I apologize for rising again but should like to add a third voice to the plea for greater use of autografts in the femoral and popliteal areas. I have one patient who has autogenous vein grafts from groin to knee bilaterally, both of which have remained open and functioning for 9 years. I believe that we probably have paid too little attention to the possibilities of this type of graft and perhaps more data should

be obtained on its use by a larger number of clinicians.

Dr. D. Emerick Szilagyi. I wish to thank the discussants for their remarks that have contributed further information about the subject of our paper.

It is undeniable that the accumulating evidence points more and more convincingly to the arterial substitute as a serious factor—perhaps the most serious factor—in the causation of late failures after femoropopliteal operations. One certainly cannot be entirely happy about the performance of the presently available plastic prostheses.

The biologic qualities of venous autogenous grafts are, of course, unexcelled. However, there are many practical difficulties associated with their clinical application. I cannot see, for instance, how one could provide the necessary quantity of autogenous vein-graft material to take the place of plastic substitutes in the femoropopliteal area. One must, moreover, bear in mind that the quality of plastic prostheses is constantly being improved. In the wake of the remarks heard today, one may wish to explore further the wider clinical applicability of venous autografts, but one will not abandon the use of plastic prostheses.

Studies on carotid artery flow

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With the extension of vascular surgery to the treatment of the extracranial portions of the carotid and vertebral arteries there has developed a renewed interest in the cerebral circulation. There is little precise information available about flow through these vessels. Total cerebral circulation has been calculated by various indirect techniques, particularly that of Kety and Schmidt,[3] and the figure usually given for normal flow with this method is about 750 ml. per minute. Flow through individual vessels cannot be measured by this technique and, to our knowledge, there are no previous reports of direct measurements of blood flow through the carotid arteries in man.

The effect of various mechanical factors such as head positioning, occlusion of other vessels supplying the brain, and the direction and volume of flow through the carotid vessels following ipsilateral common carotid occlusion have become matters of clinical importance.

The following studies were made with a more accurate and direct method of measurement of carotid artery blood flow than was available in past years.

Supported in part by Hartford Fund Grant and United States Public Health Service Grants H-5213 and H-4893.
Read at the Fourteenth Annual Meeting of the Society for Vascular Surgery, Miami Beach, Fla., June 12, 1960.

METHOD

Measurements were made with a non-cannulating electromagnetic flowmeter[2] at the time of neck dissection (usually for carcinoma). The patients did not have known cerebrovascular disease. The patients' heads were draped in such a manner that the surgeon could move them freely into various positions. The majority of patients had the internal jugular vein ligated prior to exposure of the arteries, but it is doubtful that this procedure had significant effect on the flow in the carotid vessels. General anesthesia, usually Fluothane, was used. The vessels were exposed adequately so that the application of the flowmeter probe did not distort them (Fig. 1). Temporary occlusion, which is required for base line measurements, was accomplished by constricting tapes which were placed about the vessels (Fig. 2). A typical tracing is shown in Fig. 3. Compression of the opposite carotid artery, when performed, was carried out by percutaneous digital pressure in all but one patient, in whom a bilateral neck dissection permitted direct occlusion.

RESULTS

Internal carotid artery flow was measured in 11 patients and found to vary from 289 to 494 ml. per minute, with the mean flow being 364 ml. per minute (Table I).

In 4 patients flow through both the

Fig. 1. The carotid vessels are exposed at time of neck dissection. The internal jugular vein has been ligated. Note that the external and internal carotid arteries are well separated so that the external application of the electromagnetic probe does not distort these vessels.

Fig. 2. The electromagnetic probe is shown in place around internal carotid artery. The constricting tapes about vessels are for occluding the vessels in order to obtain a base line reading of zero blood flow.

common and internal carotid arteries was measured. In these patients approximately 70 per cent of the common carotid flow went through the internal carotid artery.

After acute occlusion of the common carotid artery, the flow continued forward toward the head in 8 patients and reversed itself in 7 of the 15 patients studied. This flow ranged from 75 ml. per minute forward to 85 ml. per minute retrograde. Thus, about 50 per cent had retrograde flow in the internal carotid artery (Table II).

The effect of head position on flow through the internal carotid artery is demonstrated in Table III. Flow was consistently greater with the head in the midposition, that is, face front, than when the head was turned away from the side of dissection. Technical problems with regard to placement of the probe prevented our obtaining reliable data when the head was turned toward the side of operation.

Compression of the opposite common carotid artery resulted in an increased flow through the internal carotid in the 5 patients in whom this measurement was made.

COMMENT

There are many factors which control flow through the carotid arteries, some of which have been demonstrated by these studies. Undoubtedly different anesthetic

agents as well as different levels of carbon dioxide tension have varying effects and some caution must be used in the assumption that values obtained under anesthesia with the carotid vessels exposed are strictly comparable to values in the unanesthetized normal man. With this reservation, it would appear that our measurements are somewhat higher than would have been expected from total cerebral flow studies. Assuming the flow through the two internal carotid arteries is essentially equal (we found no significant difference in flows between the right and left side), and that the combined flow of the vertebral arteries is usually about equal to the flow through a single internal carotid, total cerebral flow should be about 3 times the flow through one internal carotid artery. On this basis the estimated total cerebral blood flow of our patients under anesthesia was about 1,090 ml. per minute.

For many years some neurosurgeons have ligated the carotid arteries for intracranial aneurysms by a 2-stage procedure. The first stage consists of common carotid ligation followed later by ligation of the internal carotid or external carotid artery. The

Table I. *Internal carotid artery flow*

Internal carotid	*Flow (ml./min.)*
Right	405
Left	326
Left	485
Right	309
Right	420
Right	494
Right	310
Right	286
Right	292
Right	393
Left	289
Mean	364

Table II. *Blood flow through the internal carotid with common carotid artery occluded (ml./min.)*

Patient No.	*Flow*	*Patient No.*	*Flow*
1.	30+	9.	43+
2.	85-	10.	32-
3.	18-	11.	23-
4.	17+	12.	72-
5.	75-	13.	34+
6.	83-	14.	50+
7.	57+	15.	23+
8.	75+		

\+ Forward.
\- Retrograde.

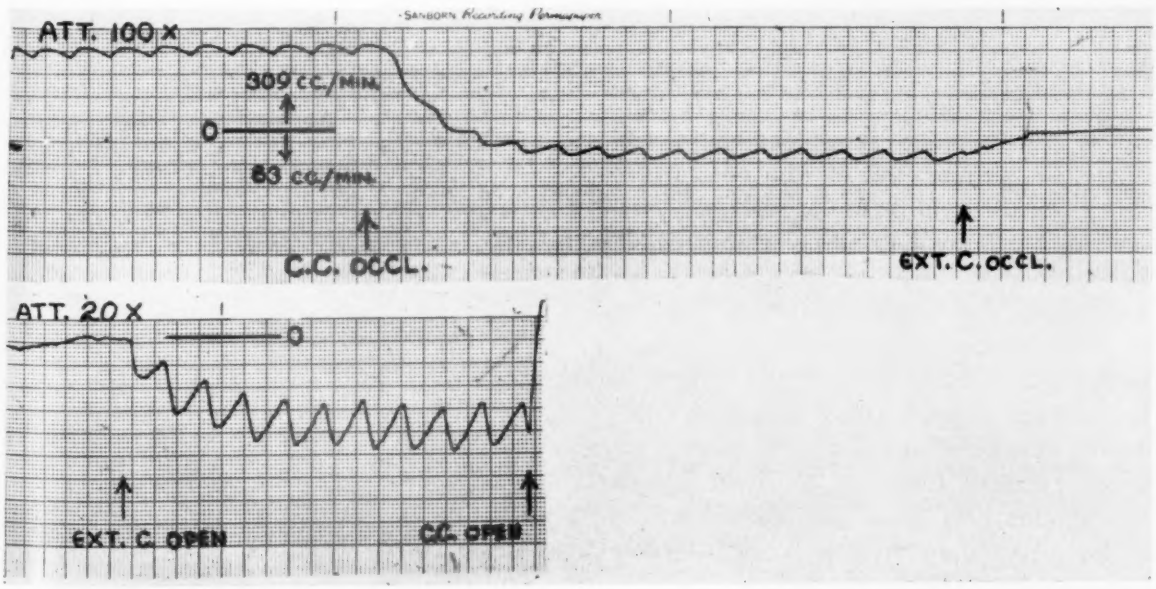

Fig. 3. Flow through internal carotid (upper tracing) before and immediately after common carotid occlusion. The external carotid was occluded to obtain a base line (zero flow). Blood flow was from internal to external carotid in this case when the external carotid was opened and the common carotid artery remained occluded. Increased amplification of recorder (lower tracing) with the vessels opened in reverse order.

Table III. *Effect of head position upon carotid artery flow*

Carotid vessel	*Flow with face away from neck dissection (ml./min.)*	*Flow with face front (ml./min.)*	*% increase*
Right internal	405	508	25
Left internal	234	298	27
Left common	320	362	13
Right internal	286	328	15
Right internal	393	454	16

rationale for this method is the knowledge that ligation of the common carotid artery results in reduction of the pressure in the corresponding internal carotid artery and the belief that early symptomatic ischemia is likely to be prevented by the maintenance of forward flow through the internal carotid artery. It is thought that this flow will support the brain until further collateral circulation has developed, at which time the second stage of the procedure is carried out. Denecke[1] in 1952 disputed the concept that blood flowed from the external to internal carotid after common carotid occlusion. He carried out studies which tended to show that flow was consistently retrograde in the internal carotid artery when the common carotid was temporarily occluded. Sweet[4] also studied this problem using pressure differentials to determine direction of flow and reported that in approximately 90 per cent of his patients (all of whom were presumed to have intracranial disease) flow was retrograde in the internal carotid when the common carotid was occluded. It appears from our studies, however, that in patients without symptomatic intracranial disease the direction and volume of flow in the internal carotid artery after acute occlusion of the common carotid artery are highly variable. Likewise, it would appear that ligation of the common carotid artery in the group that develop retrograde flow may actually result in less flow to the brain than ligation of the internal carotid.

This finding of retrograde flow is of clinical importance not only to the neurosurgeon but also to the clinician interested in carotid artery compression tests. Changes of direction of flow through the internal carotid artery may explain why there are some patients who develop cerebral effects during carotid sinus compression tests without accompanying bradycardia or vasodepression, yet do not show these effects when the common carotid is similarly compressed.[5] In these patients the specificity of sinus compression may be accounted for by the fact that some forward flow is maintained through the internal carotid with common carotid compression and not with sinus compression.

The fact that flow through the internal carotid artery is consistently reduced when the head is turned to the opposite side is also of clinical importance. There is evidence that many cerebral ischemic episodes heretofore attributed to carotid sinus hypersensitivity are actually brought about by mechanical interference with cerebral flow.[3] There is normally considerable ability to compensate for occlusion of one vessel. This is clearly shown by our results which revealed an increased flow through the internal carotid artery when the opposite common carotid was occluded by direct pressure (Table IV). Under pathologic conditions cerebral ischemia may become manifest when the carotid vessels are diseased and unable to compensate for reduced flow in the affected vessel. There may also be alterations of flow through the vertebral arteries under these circumstances but we have no data on blood flow through the

Table IV. *Effect of contralateral common carotid artery occlusion*

Patient	*Internal carotid artery*	*Flow before occlusion (ml./min.)*	*Flow with occlusion of opposite common carotid (ml./min.)*	*% increase*
G. W.*	Right	238	270	13
G. B.	Left	230	317	38
M. E.	Right	300	410	37
E. J.	Right	393	478	22
J. H.	Left	312	395	27

*Direct compression.

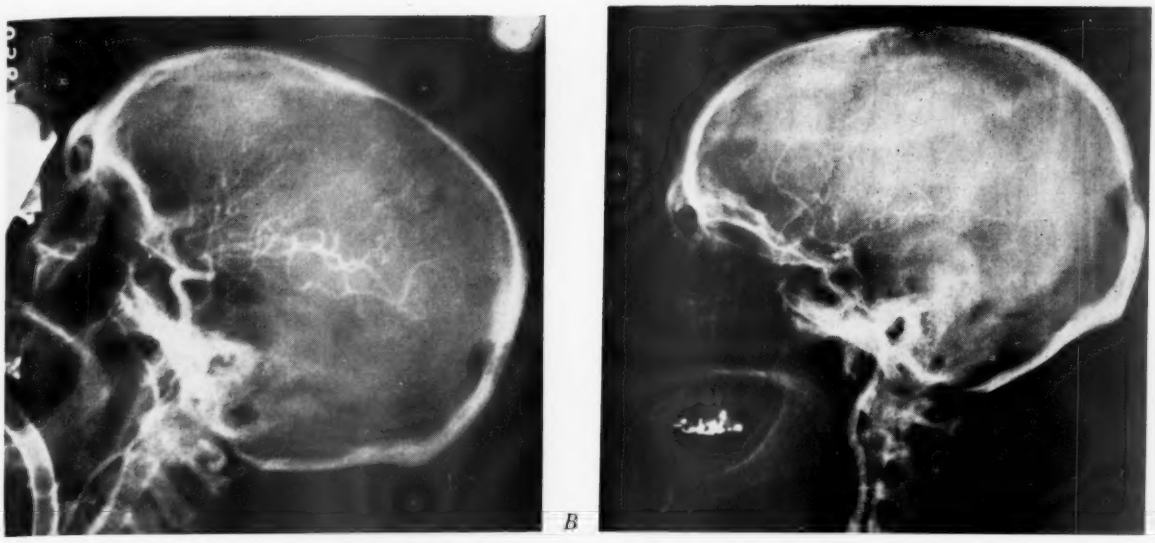

Fig. 4. *A*, Arteriogram with direct injection into the right common carotid artery shows the carotid vessels in spasm. *B*, Arteriogram with injection into the innominate artery in the same patient 2 weeks later shows a normal carotid vessel pattern.

vertebral arteries. Perhaps the increased flow in one carotid that follows occlusion of the opposite vessel is primarily mechanical and results from the drop in arterial pressure in the one hemisphere.

Compensatory mechanisms are not consistently able to overcome the loss resulting from occlusion of one vessel. This is obvious from the clinical observations that surgical ligation, atherosclerotic stenosis, or spontaneous thrombosis of one internal carotid vessel will result in definite neurologic deficit in a significant percentage of people. A distinctly unusual situation occurs when a patient can tolerate occlusion of both internal carotids without developing widespread neurologic defect. The response of the individual patient will depend on multiple factors, an important one of which is the anastomotic pattern of the circle of Willis. To illustrate how much an occasional patient can compensate, we recently found bilateral internal carotid artery occlusion and constriction of the right vertebral artery in a patient who had never had paralysis and whose only sign was slight mental deterioration. In this patient the ability of the external carotid and vertebral arteries to compensate for occlusion of the internal carotid vessels was extraordinary. The total flow was 80 per cent of normal and approximately 575 ml. per minute (Kety and Schmidt technique).*

Still another factor that may affect flow and produce symptoms is spasm. That spasm of the internal carotid artery may occur is known, but it is seldom demonstrated. A recent arteriogram which was followed by a transient hemiplegia demonstrated this very well when it was compared to a subsequent study (Fig. 4) in which a retrograde brachial catheter was used. It seems likely that the transient paralysis in this case was related to the diminished flow resulting from spasm rather than direct toxicity of the dye, since the second study did not produce spasm or paralysis although the same dye was used.

SUMMARY

1. Using an electromagnetic flowmeter we found the mean flow through the internal carotid artery in patients under anesthesia to be 364 ml. per minute.

2. When the common carotid artery was occluded, flow in the internal carotid was

*Measurements were performed by Dr. C. J. Lambertsen.

reversed in about 50 per cent of the individuals.

3. Turning of the head to the opposite side consistently resulted in reduction of flow through the internal carotid artery.

4. Occlusion of one common carotid artery routinely resulted in an increase in flow in the opposite internal carotid artery.

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Intermittent vertebral artery compression: a new syndrome

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In 1959, Cate and Scott[1] reported the relief of symptoms of arterial insufficiency of the basilar system after endarterectomy of the proximal portion of one vertebral artery. The occurrence of a similar symptom complex consisting of vertigo, syncope, tinnitus, and deafness in a large number of patients without evidence of arteriosclerosis prompted an investigation into other possible causes for vertebral artery insufficiency. This report is concerned with certain congenital anomalies of the subclavian-vertebral axis which may result in intermittent vertebral artery compression.

Our attention was drawn to the possible relation between vertebral artery insufficiency and the anatomic variations in the origin of this artery by a patient who presented symptoms of brain-stem ischemia and arterial insufficiency of the right upper extremity. A subclavian-vertebral arteriogram demonstrated what appeared to be a filling defect at the origin of the right vertebral artery and therefore exploratory operation was performed. The vertebral artery was found to arise from the posterior surface of the subclavian artery, directly behind the thyrocervical trunk. The proximal portion of the vertebral artery was almost completely occluded by external compression and angulation produced by the thyrocervical trunk and the medial border of the scalenus anticus muscle. After division of the scalenus anticus and also of the thyrocervical trunk, the compression was relieved and an excellent pulse was obtained in the vertebral artery. The patient has now been free of symptoms for 22 months. Since this observation, we have studied 28 patients who presented the chief complaint of episodic vertigo with or without other symptoms referable to brain-stem ischemia. In 17 of these cases the vertebral artery arose from the subclavian artery in common with, or at the level of, the thyrocervical trunk. In 4 other patients the left vertebral artery arose directly from the aortic arch and then entered the vertebral canal at the level of the fourth cervical vertebra. All 21 patients have improved or have been completely relieved of their symptoms after surgical treatment. Seven of the 28 patients showed atherosclerotic disease involving the vertebral-subclavian junction.

Supported in part by the United States Air Force Grant AF 41(657)-272.
Read at the Fourteenth Annual Meeting of the Society for Vascular Surgery, Miami Beach, Fla., June 12, 1960.

THE CLINICAL SYNDROME

The symptomatology of the syndrome of intermittent vertebral artery compression differs from that in arteriosclerotic occlusive disease insofar as the former syndrome is episodic in nature with periods of complete freedom of symptoms alternating with the almost explosive onset of true vertigo.

Although the time of onset of attacks is apparently unpredictable, the precipitating factors are either emotional tension or rotation and extension of the head. In either situation the neck muscles, including the scalenus anticus, are drawn tightly over the

thyrocervical trunk and subclavian arteries which produces compression of these vessels against the proximal vertebral artery.

The symptoms may vary from simple vertigo to the more complex picture of basilar artery insufficiency. The symptoms of the latter include diminished hearing of the central type with a considerable perceptive component frequently associated with the phenomenon of recruitment. Tinnitus, when present, may persist after the vertigo has ceased and in some patients is continuous.

Headache is common and is usually of the tension type, predominately unilateral and situated in the supraorbital or parieto-occipital area. In more severe cases the pain is facial in location and is a deep-seated ache, characteristic of visceral rather than somatic neuropathy.

Gastrointestinal symptoms consisting of nausea, vomiting, and explosive diarrhea may accompany the episodes of vertigo. Cawthorne[2] believes that these symptoms result from a spread of excitation from the vestibular nucleus to the adjacent vagal centers.

Visual disturbances may be present and are of the perceptive type. The patient may complain of inability to sustain prolonged periods of visual concentration or of an hallucination of flashing lights or horizontal lines. These symptoms arising from ischemia of the occipital lobe result from insufficiency of the posterior cerebral artery, a branch of the basilar system, and may occur in the presence of normal internal carotid arteries.

Paresthesia, numbness, and coldness of the upper extremity on the affected side are frequently present and are also episodic, usually in association with the symptoms of cerebral ischemia. There may be a definite vasospastic element with rapid changes in color, temperature, and sweating in response to thermal or emotional stimuli. These symptoms are an important diagnostic feature of the syndrome of intermittent vertebral artery compression since they are associated with the physical signs of subclavian artery compression by the scalenus anticus muscle.

Physical findings during the asymptomatic intervals between attacks may be limited to those seen in the scalenus anticus syndrome. Diminution or obliteration of the radial pulse usually occurs with the Adson maneuver, although in many instances an oscillometer is required to be certain that a real change is obtained. Great care must be taken not to place the arm in hyperabduction since many apparently normal individuals show a decreased pulse amplitude with the arm in this position.

The performance of the Adson maneuver may precipitate an attack of vertigo, and because of this, some of our patients refused to have the test repeated for fear of the severe symptoms which resulted. We believe the occurrence of such an attack during rotation and hyperextension of the neck to be diagnostic of the vertebral compression syndrome.

A supraclavicular bruit was present in about one-third of our patients, although in some it could be demonstrated only with changes in the position of the head. The bruit can be either systolic or continuous and is usually transmitted along the subclavian artery rather than upward into the neck.

Episodic symptoms of vertebral artery insufficiency, evidence of a scalenus anticus compression syndrome, and a supraclavicular bruit comprise the clinical features of this syndrome.

METHODS

Arteriographic studies. The anatomic diagnosis of an anomalous origin of one or both vertebral arteries can be made from arteriographic studies. Bilateral percutaneous subclavian arteriograms were carried out in all 28 cases. These studies are performed under light general anesthesia supplemented with Novocain infiltration by a modification of the techniques described by Shimidzu.[8] The needle is inserted at a point 1 inch above the clavicle and just lateral to the sternal head of the sternomastoid muscle. The tip of the needle is then directed at a spot deep to the sternoclavicular joint at an angle of approximately 45°. Eight milliliters of 50

Fig. 1. Normal subclavian-vertebral arteriogram. The vertebral artery originates 2 cm. medial to the thyrocervical trunk and rises parallel to the vertebral bodies.

per cent diatrizoate (Hypaque) is injected as rapidly as possible and a single exposure taken during the injection of the final 1 to 2 ml. of solution.

Fig. 1 shows an arteriogram with the vertebral artery arising from the normal location, about 2 cm. medial to the thyrocervical trunk and internal mammary artery. In addition, the vertebral artery arises from the ascending portion of the subclavian artery at an oblique angle and rises in a straight line, always close to the vertebral bodies. Figs. 2 and 3 demonstrate the anomalous origin of the vertebral artery seen in 17 of 28 patients with a chief complaint of vertigo. Fig. 2 illustrates a common vertebral-thyrocervical trunk. Fig. 3 shows the vertebral artery arising from behind and at the level of the thyrocervical trunk. This anomalous situation occurs in 3.03 per cent of the general population[3] and the high incidence in our cases is therefore statistically significant. In both cases the lateral displacement of the origin of the vertebral artery produces a sharp angulation in its proximal course. Fig. 4 demonstrates occlusion of the vertebral artery with rotation of the head. Fig. 5, *A* illustrates the significance of this anomaly in the production of vertebral artery insufficiency. The lateral and posterior displacement of its origin makes it vulnerable to marked compression by a taut scalenus muscle. Fig. 5, *B* shows the combined effects of scalenotomy

Fig. 2. Arteriogram which shows anomalous origin of vertebral artery from the thyrocervical trunk.

Fig. 3. Arteriogram showing anomalous origin of vertebral artery from the posterior surface of the subclavian artery, laterally displaced to the level of the thyrocervical trunk.

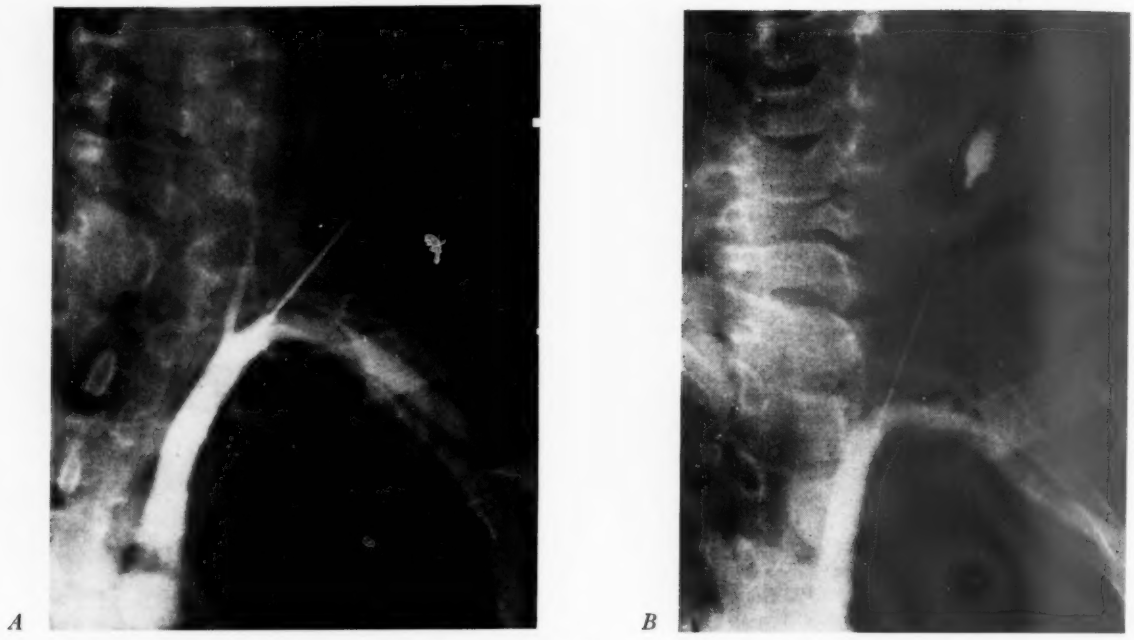

Fig. 4. *A,* Arteriogram which shows good filling of the vertebral artery with head in neutral position. *B,* Failure to fill with head rotated and neck extended.

and division of the thyrocervical trunk in allowing the subclavian artery to rotate downward and forward and the consequent straightening of the vertebral artery.

Special diagnostic procedures. Audiograms were carried out in all patients. Approximately two-thirds of them showed a significant hearing loss. Deafness, when present, was of the low frequency type and frequently was associated with recruitment. These findings are typical of a nerve type of deafness, but unfortunately will not distinguish lesions of the organ of Corti from those involving the cochlear nerve or brain stem. Since the internal ear derives its blood supply from the internal auditory artery, a branch of the basilar or vertebral, and the brain stem is supplied directly from the basilar artery, it is possible for either or both sites to become ischemic with vertebral artery insufficiency. The most striking change in auditory function in these patients is a perceptive hearing loss which produces a greater disability than might be expected from the audiometric study. It is interesting that postoperatively there is frequently an improvement in speech perception which is only occasionally accompanied by a corresponding improvement in the audiometric examinations.

Circulatory studies of both arms were carried out pre- and postoperatively in most patients. The impedance plethysmograph was used since it yields quantitative estimates of arm blood flow as well as volume-pulse contours. A grossly abnormal tracing was obtained in 19 of 20 patients studied. It is interesting that the diagnosis of subclavian artery compression could be made on several patients in whom the Adson test was normal. For this reason we believe the plethysmographic tracing to be a more reliable diagnostic test than the Adson maneuver. Fig. 6 illustrates a normal upper arm plethysmogram and also a tracing from a patient with subclavian-vertebral artery compression. The marked dampening of the volume-pulse contour is well demonstrated.

The symptoms of cerebral ischemia are similar to those seen in other diseases involving the brain stem such as cerebellopontile angle tumors and aneurysms of the basilar artery. For this reason a rather elaborate study is justified in any patient who complains of vertigo. Each of our patients was subjected to spinal puncture, caloric test-

ing, audiometric examination, and in some cases, an electroencephalogram. In several instances, roentgenograms of the skull were also taken and pneumoencephalography performed. Every patient was then carefully evaluated by our neurologist before arteriographic studies were begun.

Surgical technique. The operative approach is planned to expose the subclavian artery and its branches from the point at which it leaves the superior mediastinum to the point at which it disappears between the first rib and the clavicle. This is accomplished through a partial collar incision which extends from behind the posterior border of the sternomastoid muscle to just across the midline. Both heads of the sternomastoid are mobilized so that the sternal head can be retracted medially and the clavicular head laterally. The strap muscles are likewise mobilized and retracted. The deep cervical fascia is then incised, as well as the carotid sheath, allowing mobilization of the internal jugular vein, carotid artery, and vagus nerve.

At this point in the dissection it can be seen that the posterior portion of the carotid sheath is fused medially to the prevertebral fascia and laterally to the deep cervical fascia which also invests the scalenus anticus muscle. The combined musculofascial membrane crosses the subclavian artery so that the entire membrane must be divided to effect complete decompression of the proximal subclavian artery. Routine scalenotomy without division of the deep cervical fascia and posterior carotid sheath may lead to failure of relief of the dorsal outlet syndrome as well as vertebral artery insufficiency.

After division of the scalenus anticus, the entire subclavian artery is mobilized by division of its cervical branches. The thyrocervical trunk must be sectioned since it draws the subclavian artery upward and backward, angulating the proximal vertebral artery. After this maneuver, the subclavian artery rolls forward and downward, bringing the orifice of the vertebral artery into view (Fig. 5) with restoration or improvement in the vertebral pulse.

RESULTS

Seventeen patients with the syndrome of intermittent vertebral artery compression due to an anomalous origin of the vertebral artery from the subclavian artery have been surgically treated and followed for 3 to 28 months. The anomaly was unilateral in 13 patients and bilateral in 4. All were subjected to unilateral vertebral mobilization with selection of the side associated with the hearing loss in those in which both sides were involved.

Sixteen of 17 patients have been improved or completely relieved of vertigo, nausea, and vomiting up to the time of this report. The one patient with a poor result was one of the first in this series and was treated before the importance of division of the thyrocervical trunk was appreciated. Tinnitus has disappeared in all but 2 patients and in these it is now intermittent rather than continuous. Preceptive hearing has improved in 6 cases whereas objective improvement in the audiometric examination (more than 15 decibels) has occurred in only 2.

All of the patients with symptoms referable to the upper extremity have been relieved and bruit, if present preoperatively, has disappeared. Postoperative plethysmograms show a return to a more normal pulse volume

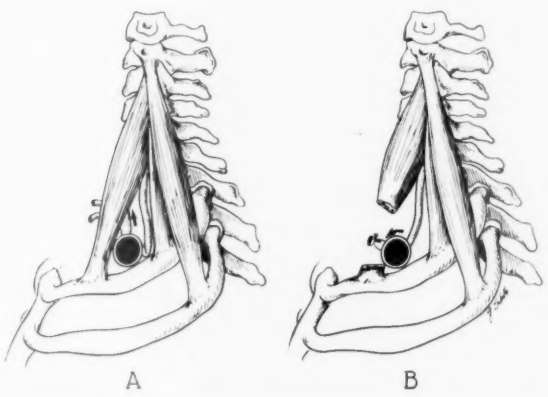

Fig. 5. Diagrammatic representation of the angulation in proximal vertebral artery which results from *A*, abnormal origin behind thyrocervical trunk and *B*, correction of this anomaly by division of scalenus anticus and thyrocervical trunk. The subclavian artery rolls forward so that the vertebral now arises from its superior surface.

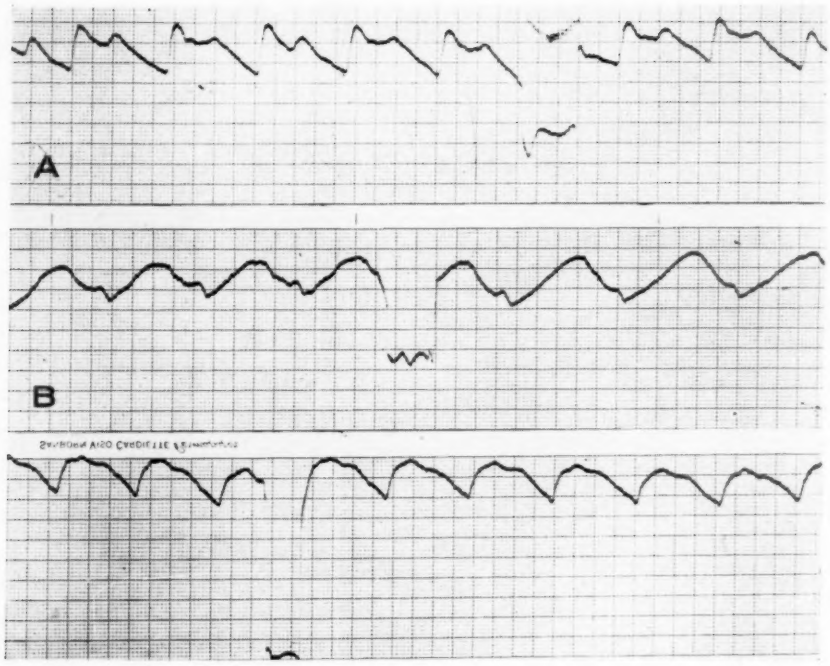

Fig. 6 *A,* Normal forearm impedance plethysmogram. Note rapid systolic rise time. *B,* Abnormal plethysmogram in patient with subclavian artery compression. The systolic rise time is markedly prolonged indicating dampening of the volume-pulse contour.

curve and usually a significant increase in arm blood flow.

The principal postoperative complication has been a tendency for the patient to stagger for a period of several weeks. This was not accompanied by any vertigo and was described as a new symptom by most patients. These symptoms were accentuated by either forceful rotation or extension of the neck. We first thought that this symptom was due to vascular spasm in the brain stem secondary to surgical trauma of the vertebral arteries but were forced to abandon this concept because of the absence of vertigo or other signs of cerebral ischemia. We then noted that the periods of staggering were associated with spasm of the sternomastoid muscle on the side of operation and therefore injected this muscle with procaine. This offered immediate, though temporary, relief of both the muscle spasm and the staggering gait. We now believe that this complication is due to stimulation of the myotactic reflexes in the neck muscles consequent to surgical trauma.[7] We have also observed that this distressing symptom spontaneously disappears at about the same time as the induration and tenderness in the operative area. There were no deaths in this series.

COMMENT

Vertigo is an exceedingly common complaint of patients who consult either neurologists or otolaryngologists. Many patients use the word "dizzy" to encompass everything from a feeling of light-headedness to actual syncope, so that a careful history is required to elicit the symptoms of true vertigo. Cawthorne[2] describes vertigo as an "hallucination of motion" either of the patient with respect to his environment or of the environment itself. In many cases the hallucination is so strong that the patient will suddenly fall forward or to one side. Nystagmus, nausea, and vomiting are frequent, but they are not essential to the diagnosis of vertigo.

The relation between vertigo and vertebral artery insufficiency has been previously reported. Ford[5] described a patient with epi-

sodic vertigo which resulted from intermittent obstruction of the vertebral artery due to a defect in the odontoid process and excessive mobility of the second cervical vertebra. The patient was symptom-free after fusion of the upper cervical spine. Tatlow and Bammer[10] describe 3 cases of vertigo associated with vertebral compression from cervical spondylitis. They and de Kleyn and Versteegh[4] carried out studies on the relation of vertebral artery flow to head rotation in postmortem material. In both reports the vertebral artery could be completely occluded by turning the head backward and to the opposite side. We believe that these represent uncommon causes of vertebral artery compression whereas the anomalous origin of this artery is very frequent. It is highly significant that although this anomaly occurs in only 3 per cent of the general population we observed its presence in over 60 per cent of all cases studied and over 80 per cent of the nonarteriosclerotic group. Actual occlusion of the vertebral artery was difficult to demonstrate arteriographically because the technique of percutaneous puncture seemed to preclude extensive motion of the head. In one patient (Fig. 4) this maneuver was accomplished and resulted in failure to visualize the vertebral artery with the head in the Adson position. On the other hand, diminution or complete obliteration of the vertebral artery pulse was demonstrated in each patient at the time of operation.

The exact mechanism by which vertebral artery compression leads to the symptoms of vertigo, tinnitus, and deafness is speculative. Ischemia of the labyrinth might occur since the latter is supplied by the internal auditory artery which may occasionally rise directly from the vertebral before it joins to form the basilar. It would therefore be necessary to postulate an additional intracranial anomaly to account for the predominately unilateral symptoms of this syndrome.

A more acceptable explanation is that unilateral vertebral compression produces a certain degree of ischemia throughout the brain stem and in addition there is vasoconstriction of the internal auditory artery. Sympathetic fibers from the cervical ganglion pass directly in the sheath of the vertebral artery and accompany this vessel and its branches. Spiegel and Sommer[9] have demonstrated changes in labyrinthine function after stimulation of the cervical sympathetics. Mechanical compression of the vertebral artery and its plexus could therefore result in spasm of the internal auditory artery in much the same way that compression of the subclavian artery and brachial plexus by the scalenus anticus muscle results in vasospastic disorders of the hand.

We have noted that the nerve fibers from the cervical plexes to the vertebral artery are invariably severed during surgical mobilization of this vessel and may be important in obtaining relief of symptoms. In this regard Passe[6] has reported the successful treatment of Menière's syndrome by cervical sympathectomy, including stripping of the vertebral artery. This concept of general brain stem ischemia plus spasm of the terminal branches of the vertebral artery would also explain the associated symptoms of nausea and vomiting as due to a direct effect on the vagal nucleus. On the basis of this hypothesis, we now include stripping of the vertebral plexus as a part of the operative treatment.

SUMMARY

The cases of 17 patients with vertigo, tinnitus, deafness, supraclavicular bruit, and a diminished radial pulse are reported. All the patients had an anomalous vertebral artery. All had subclavian-vertebral arteriograms preoperatively. Each patient showed an anomaly of the vertebral artery system which allowed intermittent compression of either the origin or cervical course of the artery. The compression was usually aggravated by rotation or hyperextension of the neck. In most cases, the vertebral artery arose at the level of the thyrocervical trunk and the compression was relieved by section of the scalenus anticus muscle and by division of the inferior thyroid artery.

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Massive congenital solitary cyst of the liver in infants

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According to Henson and associates[7] and to Desser and Smith,[3] Bristowe, in 1856, was the first to report a case of congenital hepatic cyst and he noted the association between cystic disease of the liver and that of the kidney. The majority of cases encountered in a survey of the literature are part of a diffuse multicystic disease involving not only the liver, but also other organs.[6, 7, 12] Solitary cysts of the liver are a distinct and separate entity, and their incidence is far lower than that associated with multiple cysts or widely separated cystic manifestations. Modern writers have estimated that the number of cases reported approximates 250,[3, 13] occurring mostly in adults. Many solitary cysts have been incidental operative or necropsy findings.[3, 4, 7]

Few cases have been reported in children, and operations for them have been fewer still. Desser and Smith,[3] out of a total of 7 cases in children, presented 2 which occurred in infants under 3 days of age. Both had come to postmortem examination without operation. Eliason and Smith[4] estimated that only 25 cases had been reported in children under 13 years of age up to 1944 and Desser and Smith[3] could find only 38 reported before 1956. Among the children operated upon early in life were those of Montgomery[12] (6 months), Stoesser and Wangensteen[21] (7 months), and Munroe[15] (9 months).

Received for publication April 22, 1960.

In size, hepatic cysts have varied from several centimeters in diameter to gigantic proportions.[16, 23] Many writers have referred to the older reports of cases in which the size of the cyst in the unborn child created profound dystocia. Probably the most famous of these reports is that of Witzel written in 1880.[14, 15, 20, 21, 24] In this rather macabre case the infant had been inadvertently decapitated by traction incident to attempted delivery and it was necessary for Witzel to use the perforator to deliver the remainder. This, however, was a case of diffuse cystic disease.

Symptoms, in the absence of complications, have been produced by the presence of an abdominal space-consuming mass, with distortion and displacement of the viscera. The occurrence of the complications of strangulation, rupture, jaundice, and hemorrhage reported in adults has not been recorded in children.[2, 10, 15, 17, 24]

The correct diagnosis has rarely been made before operation. Not over 3 cases in all age groups have been diagnosed prior to operation.[1, 9, 15, 21] In children there has been only 1 correct diagnosis, that made by Eliason[4] in a child 2½ years of age. With the larger cysts roentgenograms invariably show considerable distortion and displacement of the hollow abdominal viscera, usually downward and to the left. Frequently other cystic abdominal lesions are considered, as in the present case. Ovarian, mesenteric, and renal cysts, as well as

hepatomegalia and hydrops of the gall bladder have been suspected most often.[2, 5, 15, 19, 21] A high index of suspicion, the x-ray signs of hollow-viscus displacement, and the paucity of symptoms should further proper preoperative interpretation.

The site of origin is almost consistently the undersurface of the right lobe. Most reported cysts have been pedunculated, and torsion has occurred occasionally as a consequence. Some cysts have been loculated. The cysts are either lined with a flattened cuboid epithelium suggestive of bile duct lining, or have only a dense fibrous layer devoid of epithelium, as in our case.

Many theories have been advanced concerning etiology. Most writers favor the theory that the cysts arise either from faulty fusion of the ductal elements or from accessory or aberrant bile ducts.[8, 12, 13, 21-23]

Ideally, complete extirpation is the preferred method of treatment. Only a few cysts, however, have lent themselves to total excision.[4, 7, 23] The majority have been treated by marsupialization or some variation of that procedure. This method, although it has resulted in complete cures, has as its main disadvantage the long period of drainage with persistent sinus frequently associated with it. Escharotic solutions have been injected into the residual drainage area in an attempt to sclerose it. Drainage lasted for 37 months in one case, according to Munroe.[15] Recently, Manheimer[11] advocated internal drainage with an anastomosis of the cyst to the stomach similar to that used in the treatment of cyst or pseudocyst of the pancreas. The use of this method of management has not yet been reported in children, but conceivably could become the method of choice in cysts not amenable to total extirpation.

CASE REPORT

Baby girl L., prematurely born at 7 months, had been delivered by vaginal birth at the DePaul Hospital on Oct. 23, 1950. Her birth weight was 3 pounds, 6 ounces. It was noted immediately after delivery that the child had a tremendous abdomen. Her general condition remained precarious for many weeks. Convulsions were frequent and during these, severe cyanosis often necessitated oxygen thearapy. There was some initial weight loss in excess of that anticipated physiologically. Although the baby began to gain, it was obvious that the weight increase was due primarily to progressive abdominal enlargement without evidence of general increase in over-all size. There was, in fact, concomitant wasting of the extremities. The infant progressed slightly, if at all, for weeks. Anemia required repeated small transfusions.

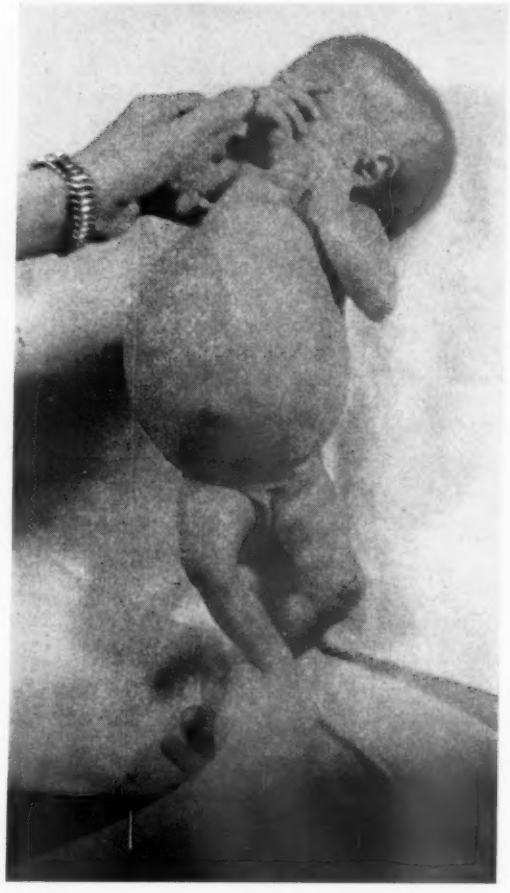

Fig. 1. Photograph of the patient on the day prior to operation. Note the distended abdomen and the relative size of the child compared with the nurse's hands.

Plain abdominal films obtained on October 24, the day after birth, revealed a huge space-occupying lesion on the left side which displaced the entire intestinal tract toward the right. The liver shadow was noted to be relatively large but not abnormally so for a newborn premature infant. A diagnosis of possible kidney tumor or cyst was made, but the possibilities of mesenteric or ovarian mass were also suggested in the radiologic report. One month later a repeat abdominal film revealed the mass to have increased in size propor-

tionately more than the infant had grown. The nature of the mass again could not be determined.

Consequently, and because of continual abdominal enlargement, on November 27 retrograde pyelography was attempted. The bladder was normal, as were the ureteral orifices. It was impossible to introduce catheters successfully into either ureteral orifice, although urine was seen to be issuing from both sides. On November 30 additional pediatric consultation was requested. At that time there was noted a huge mass predominantly on the left of the abdomen with displacement of the hollow viscera to the opposite side. Because the infant was losing ground and was dyspneic, it was the opinion of both pediatric and urologic consultants that the patient should undergo abdominal exploratory operation.

Surgical consultation was requested on December 6, when the infant was 44 days old. At that time examination showed an emaciated, cachectic infant who exhibited considerable respiratory difficulty and moderate cyanosis (Fig. 1). There was a huge, cystic abdominal mass occupying the entire abdomen but bulging predominantly on the left side. Percussion was flat on the left, tympanitic on the right. There was a large, tense, umbilical hernia which was protruding. Further transfusions were recommended and laparotomy was to be performed as soon as the baby's condition improved satisfactorily. At the time of surgical consultation it was obvious that the child's condition was deteriorating rapidly. The possibilities considered were mesenteric, ovarian, or kidney cyst. Several additional small transfusions were given in the next 24 hours.

The night before operation it was noted that the mass had completely moved from its former predominantly left-sided position to the right side. Repeat x-ray films confirmed the clinical impression and this demonstrated mobility seemed to exclude the possibility of renal cyst (Fig. 2).

On Dec. 7, 1950, under ether-oxygen anesthesia, exploration was begun through a vertical abdominal incision. As soon as the abdomen had been opened, a huge, lobulated thin-walled, tan-colored cystic structure containing thin, brown fluid extruded spontaneously out upon the abdominal wall (Fig. 3). It was a massive, pedunculated, irregularly lobulated cyst emerging from the inferior surface of the right lobe of the liver lateral to the falciform ligament (Fig. 4). The latter was distorted and tremendously elevated by the cyst. The cystic tumor extended about 2.5 inches into the hepatic substance. Its pedicle at the border of the liver was approximately 2.5 inches in diameter. The gall bladder was normal, as were the other abdominal viscera. An additional interesting finding was the incarcerated umbilical hernia, filled with a protuberant portion of the cyst which conformed to the contour of the hernia sac. There were no additional cystic abnormalities of the liver or of the kidneys.

The child's condition at operation was precarious, and she showed rapid deterioration despite the administration of intravenous fluids and 25 ml. of whole blood. Accordingly, it was considered unwise to attempt the more definitive and desir-

Fig. 2. Photograph of abdominal x-ray film which shows huge mass on right displacing hollow viscera to the left. This situation, noted the day before operation, was a complete reversal of the previous position of the cyst. It had originally been on the left, displacing the viscera to the right.

Fig. 3. Photograph taken at operation. Note the pedunculation, the irregular contour of the cyst, and the clear intra-umbilical portion on the superior surface.

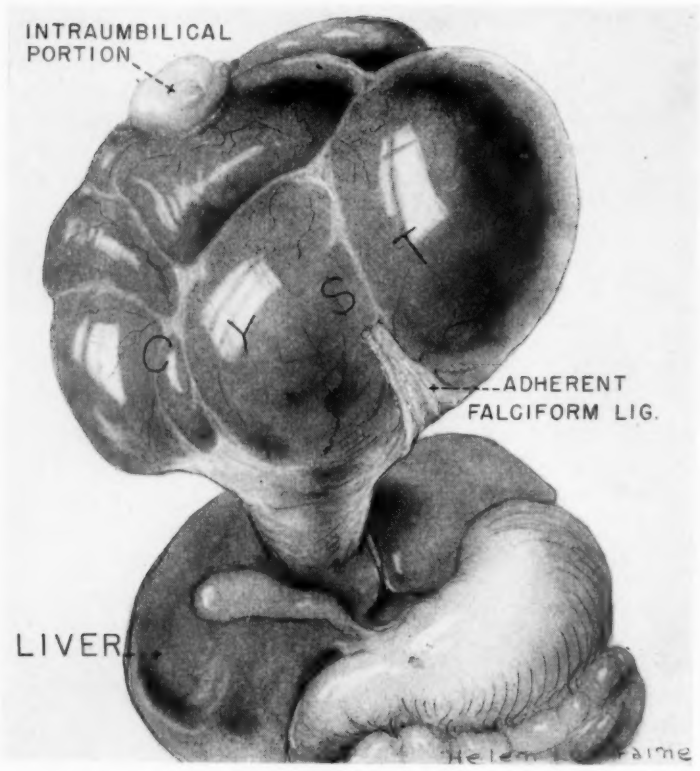

Fig. 4. Operative findings and technique, somewhat diagrammatically drawn. Note the position of the falciform ligament.

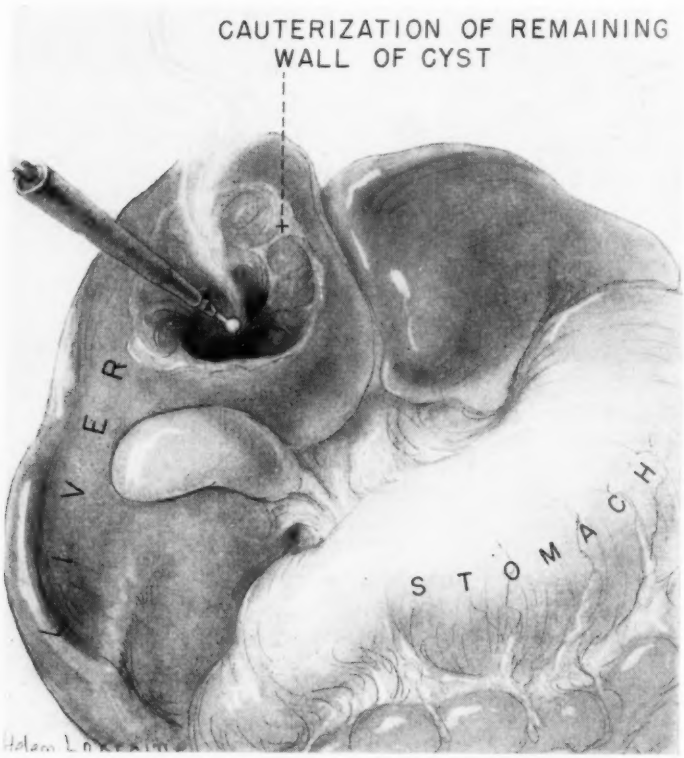

Fig. 5. Procedure used for intrahepatic portion of cyst after excision of major extrahepatic part.

able procedure of complete extirpation of the cyst with enucleation of the lining of the intrahepatic portion. The cyst was quickly excised at its junction with the liver, and the entire intrahepatic cavity lightly desiccated with the Bovie coagulation unit after the fluid had been found chemically not to contain bile (Fig. 5). This was considered preferable at the moment to marsupialization with its attendant evils. The wound in the loose redundant abdominal wall was closed quickly, and the patient's condition began to improve strikingly as soon as manipulation was discontinued. The condition of the child was relatively good within a few hours.

Pathologic examination revealed a huge, thin-walled cyst still containing 200 ml. of slightly blood-stained brown fluid. On distention with saline the total capacity of the portion removed was found to be 700 c.c. At the point where it entered the liver its wall measured 0.8 cm. in greatest thickness and had a gelatinous appearance, with intermixed reddish and brown areas. In most regions, however, it was paper-thin with superficial external lobulations. Microscopically, the outer surface was found to be covered with peritoneum. Internally the cyst was lined with flattened connective tissue cells and in some areas there was hyalinization just beneath these (Fig. 6). In other areas there was loose myxomatous tissue with some mucoid degeneration. Scattered throughout the wall were occasional areas of fatty tissue and a number of branched, tortuous, and dilated bile ducts, some of which showed proliferation and a tendency to minute cyst formation. Some of the bile ducts were immediately surrounded with loose myxomatous connective tissue. There was marked congestion throughout. The pathologist's diagnosis was "congenital cyst of the liver."

Initially after operation the baby's weight dropped back to slightly less than 3 pounds. However, there was steady general improvement after laparotomy, and the wound healed uneventfully. The baby was discharged from the hospital on December 29. Weight gain had been progressive and general vigor gratifyingly increased.

The patient was followed in the office and improvement was uninterrupted. It was noted after several months that she had a hemihypertrophy of the body and extremities. Otherwise, however, she continued to develop normally both mentally and physically. When last seen in 1959 she was a normal, healthy child in her tenth year, but the disproportion between the 2 sides of the body and extremities was still evident.

COMMENT

The case presented would seem to have much in common with those of congenital solitary hepatic cysts previously reported. There was pedunculation, origin from the depth of the inferior surface of the right lobe, and lack of definitive lining membrane. The patient was, as far as could be ascertained, the youngest and smallest to be operated upon for solitary liver cyst. The child has now been followed for over 9 years postoperatively. Although perhaps not preferable to total extirpation, the method employed was successful. It consisted essentially of excision of all the extrahepatic cyst with desiccation of the intrahepatic portion. The method was necessitated by the grave urgency of the child's condition, and it apparently represents an unusual variation of previously described techniques. It seemed preferable to marsupialization with its attendant evils, although internal drainage may ultimately prove to be efficacious in cases of cysts not amenable to complete surgical excision.

CONCLUSION

A unique case has been presented of a premature infant successfully operated upon

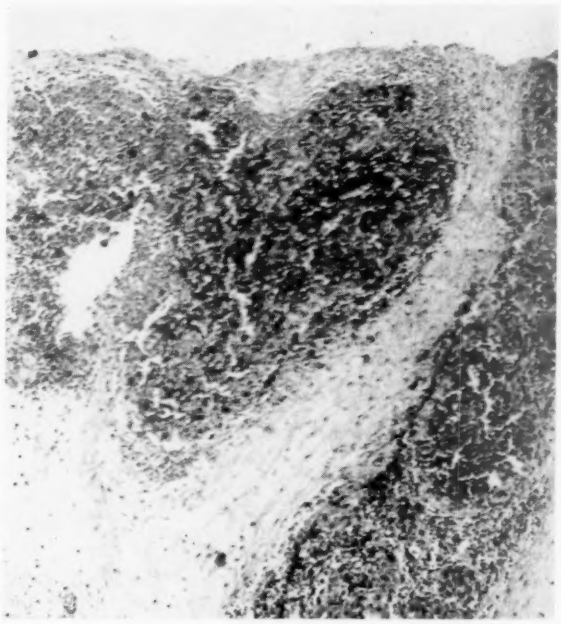

Fig. 6. Photomicrograph which shows absence of epithelial lining. This section from the neck of the cyst reveals also the clumps of underlying hepatic tissue infiltrated with red blood cells.

for a huge solitary congenital cyst of the liver. This is believed to be the youngest and smallest patient to undergo a successful operation for this condition. The extrahepatic portion of the cyst was removed and the lining of the intrahepatic portion destroyed with the electrocautery.

We are indebted to Drs. Arnold Strauss and Robert Faulconer and their associates for their assistance with the photographs and photomicrographs.

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The successful separation of pygopagous twins

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The separation of Siamese or conjoined twins has long been a surgical challenge. Frequently, successful separation either has been precluded by the nature of the conjoining or death has occurred before an operation could be performed. The survival of one twin is unusual and the survival of both is a rarity.

Statistics on the separation of conjoined twins are not accurate. Some cases are reported only by the lay press. To the best of our knowledge, 9 conjoined twins had been separated with survival of both before October, 1957, when we successfully separated the pair here reported.[1, 3-5, 7-12] One or both twins in some reported cases subsequently died. Since October, 1957, an additional set of conjoined twins has been separated.[6] An excellent review of the status of surgery for conjoined twins was presented by Wilson and Storer[12] in 1957 when they reported on their 3 experiences.

This report concerns the successful separation of pygopagous twins and their subsequent courses for 33 months. Both are now alive and well. References to the separation of pygopagous twins are made by Aird,[1] who refers to a report by the lay press, by Ochsner[12] in a cinema, and by *Time* magazine.

CASE REPORT

Pamela and Patricia were 7-day-old white pygopagous twins when they were admitted to The Children's Hospital of Philadelphia on Oct. 3, 1957.

A para ii, gravida iii woman was delivered vaginally of the twins by Dr. William Dolan at the Mercy Hospital in Rockville Center, Long Island, New York, after a 5-hour labor. They weighed 14 pounds (Fig. 1). The children were in good condition although the smaller of the two infants was noted at times to have a grayish pallor, to have rapid respirations, and to maintain a pulse between 140 and 160 per minute. It was established that there was good innervation to each extremity, that there were 2 separate urinary streams and a single vulva. Separate colons emptied into a common anus (Fig. 2).

On admission to The Children's Hospital of Philadelphia the twins had a combined weight of 13 pounds, 7 ounces. Physical examination revealed infants of unequal size united posteriorly in the sacral and perineal regions. The large twin, Pamela, appeared vigorous and no other positive physical findings were noted. The pulse rate was 116 per minute, the respiratory rate 30 per minute, and the blood pressure was 90 mm. Hg systolic in the arms and legs. The smaller child, Patricia, had a systolic blood pressure of 85 mm. Hg, a pulse of 150, and a respiratory rate of 80 per minute. She was frequently noted to be cyanotic and she appeared to be less vigorous than her twin. A harsh, early systolic murmur was audible to the left of the sternum and could be heard bilaterally on the posterior chest wall. There

Received for publication July 14, 1960.

Fig. 1. Twins on operating table. Weight is 13 pounds, 7 ounces.

was no hepatomegaly or splenomegaly and the chest was clear.

Electrocardiographic tracings were not identical, but both showed normal patterns for newborn infants, namely, a right axis deviation and evidence in the precordial leads of some right ventricular enlargement. Roentgenographic examination of the twins prior to their separation was not satisfactory for evaluation of cardiac size because they could not be properly positioned. Grossly the hearts appeared to be of normal size. Dr. Sidney Friedman, the cardiologist, was unable to establish a cardiac diagnosis but believed that there was no contraindication to an operation and that no cardiac therapy was indicated. A complete cardiovascular study of the twins and subsequent evaluation of Patricia will be reported.[2]

Hematologic study of Pamela revealed a hemoglobin concentration of 16.2 Gm., a red blood cell count of 4.74 million, and a white blood cell count of 14,850 with 39 per cent neutrophils and 61 per cent lymphocytes. Patricia's hemoglobin concentra-

Fig. 2. Conjoined perineum of twins with single vulva and anus.

tion was 16.7 Gm., red blood cell count 5.22 million, and white blood cell count 12,150 with 40 per cent neutrophils, 54 per cent lymphocytes, 2 per cent monocytes, and 4 per cent eosinophils. Both infants had group A, Rh positive blood.

Roentgenographic examination showed that the babies were joined by soft tissue in the distal sacral and perineal regions (Fig. 3). Although no bony union was demonstrated, they were rigidly attached. There were only 4 sacral segments visualized in the smaller twin.

A single intravenous injection of 7 ml. of 50 per cent Hypaque in the larger infant produced a satisfactory urogram in both infants. Bilaterally functioning kidneys were present in both infants. Each baby was found by cystography to have a normal bladder and normal urethra (Fig. 4).

Barium enemas were performed through the common anus into the separate colons (Fig. 5). These films showed 2 colons of normal appearance although the rectosigmoid of one extended beyond the midline of the fused skeleton into the perirectal space of the other.

Surgical separation was accomplished on Oct. 5, 1957, when the infants were 9 days old. Each infant had an anesthesiologist and an assistant anesthetist with no other duties. One attendant was assigned to each infant to administer intravenous fluids. The surgeon was assisted by a team of 3 and an additional team of 3 stood by to receive the larger twin after separation. A neurosurgeon and a plastic surgeon were members of the operating group, should their particular counsel be needed. Each team of surgeons had its own scrub nurse and circulating nurse, while a fifth nurse weighed the blood loss.

A cut-down was placed in the arm of each infant. Eight milligrams of succinylcholine was given intravenously to the larger twin who was awake while intubation was carried out. There was insufficient relaxation in the smaller twin for intubation, so cyclopropane anesthesia was then administered to both and intubation was subsequently carried out in the smaller one. Both infants were prepared with pHisoHex from the nipple line to the feet and sterile drapes were applied.

Catheters were sutured into place in each urethra and each colon. A midline incision was made between the urethras, and the mucocutaneous junction of both anus and vulva was cut in the midline. Each urethra was dissected free and retracted laterally with the catheters in place. The vagina was a single structure which appeared to belong to the smaller infant. It was divided to give half to each child until the uterus came into view. It belonged to the smaller twin.

A large transverse vein which appeared to be the main venous connection between the twins was ligated and divided as was a smaller artery. The terminal segment of the sacrum was found to be fused and was divided with a knife. Bleeding from the divided sacral bone was brisk. Weighed blood loss was replaced one-half in each child during the procedure.

The larger twin was immediately transported to another operating room for closure of the wound which was accomplished by swinging a skin flap from one of the buttocks to the perineum. At that time the

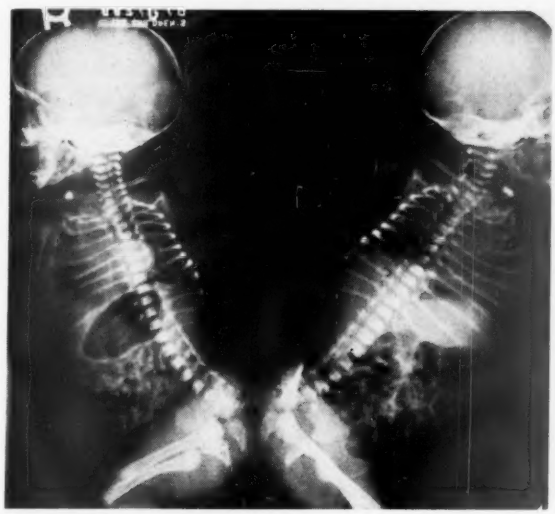

Fig. 3. Skeletal roentgenograms which show no apparent bony fusion, although bony union existed at the sacrum.

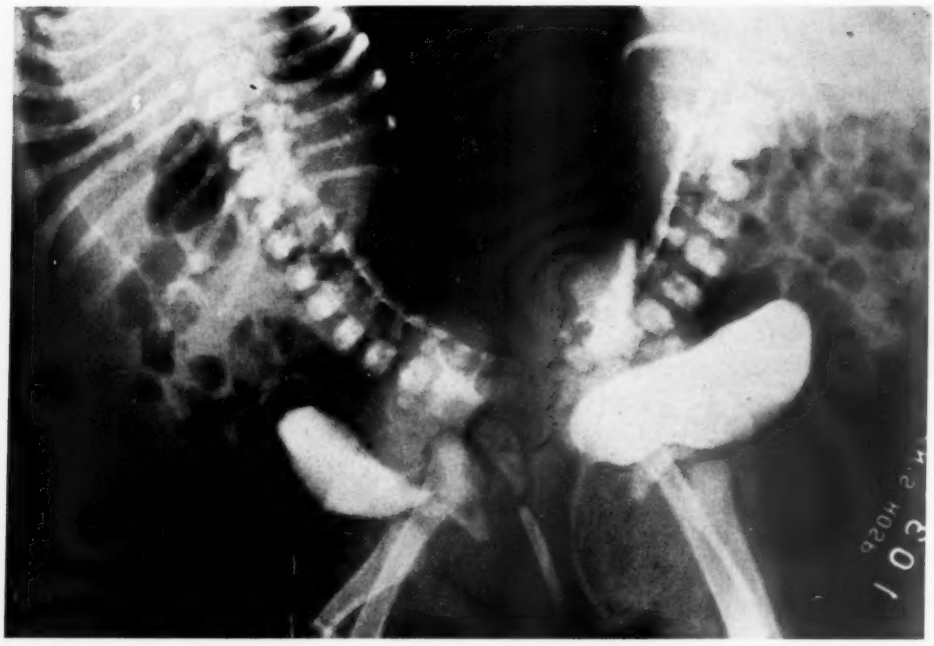

Fig. 4. Cystograms which indicate separate lower urinary tracts. The intravenous pyelograms were normal.

Fig. 5. Barium enemas showed the rectal ampulla of one twin to lie in the perirectal space of the other.

smaller twin appeared dusky. The heart sounds became faint and then ceased a few seconds later. Cardiac massage was instituted through a left fourth intercostal thoracotomy approximately 30 seconds later. The heart was flabby. Fifty milliliters of blood was given rapidly and cardiac massage was begun immediately. After several minutes of massage 2 ml. of 1 to 10,000 epinephrine was injected into the left ven-

tricle. A good heartbeat was established almost immediately and the baby soon reacted by breathing spontaneously and by moving her extremities. Further support was given with blood and intravenous calcium chloride.

The open area of the perineum and buttocks of the smaller twin measured 5 by 6 cm. The skin edges were brought together, leaving a 2 cm. defect in the center, and the vagina was sutured in place with no attempt to form a tunnel. The chest incision was then closed. The children received a total of 235 ml. of blood before separation.

Both infants were put in Isolettes* with oxygen and full humidity and taken to the recovery room. The postoperative courses of the infants were remarkably uncomplicated. They were initially given penicillin and streptomycin intramuscularly. This was later changed to oral Erythromycin and then to Gantrisin. The patients received 5 per cent glucose and some electrolytes intravenously initially and on the first postoperative day took glucose water by mouth. Half-strength skimmed milk feedings were begun the next day and the formula was gradually enriched and increased. Hemoglobin levels were followed and both patients received small blood transfusions as indicated.

Patricia weighed 5 pounds, 13 ounces, on October 7, the second postoperative day, when the chest tube was removed. The wound healed well and on October 16, the stitches were removed. The child continued to have a cardiac murmur during the first postoperative week but on October 24, the cardiologist heard no murmur. The child appeared to be vigorous and pink with a rapid respiration rate. On October 24, the nineteenth postoperative day, the child was discharged to her parents weighing 6 pounds, 13½ ounces. A small, unhealed defect remained next to the anus.

Pamela weighed 7 pounds, 5 ounces, on October 7. On October 23 a plastic repair of the perineum was performed to correct the defect left when the skin flap sloughed. The postoperative course was smooth except that the anal orifice prolapsed occasionally as did one side of the vaginal mucosa. These were easily reduced. On November 9, the thirty-fifth postoperative day, Pamela was discharged. She weighed 9 pounds, 3 ounces. Although not completely healed, the perineum was in good condition.

Pamela has remained well for the 2 years and 9 months since her original operation. A minor plastic procedure was undertaken on the perianal skin on one occasion. Her only difficulty is recurrent constipation which resembles that seen in some youngsters who have undergone an abdominoperineal pull-through procedure for imperforate anus.

Patricia went into cardiac failure when her weight had reached 12 pounds and was given digitalis with good effect. In 1960, she was readmitted to The Children's Hospital of Philadelphia for cardiac study and on the basis of angiocardiology and cardiac

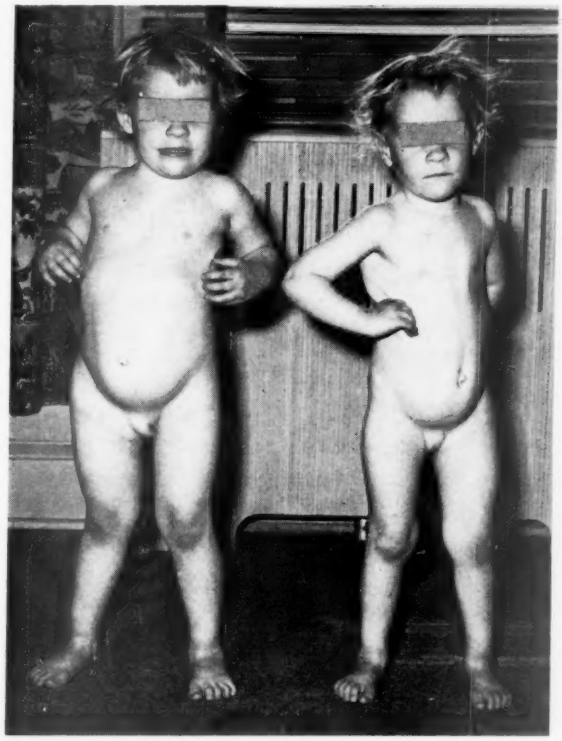

Fig. 6. Twins 33 months postoperatively.

*Air Shields, Hatboro, Pa.

Fig. 7. Perineum of larger twin. Perirectal scarring adds to difficulties of normal bowel habit.

Fig. 8. Perineum of the smaller twin whose bowel control is normal.

catheterization, the diagnosis of tetralogy of Fallot was established.[2]

At present both children (Fig. 6) appear and behave normally in every way except for the appearance of the perineums (Figs. 7, 8). Orthopedically, the only treatment they have had thus far has been corrective shoes. The pelves of both youngsters originally seemed rotated from the position of attachment during in utero life, but this is not especially discernible now, even in their gait.

DISCUSSION

The success of the separation of conjoined twins reported here is to a great extent due to the preoperative planning. The emotional hazards and tensions associated with an operation such as this are not inconsiderable and we therefore went over the mechanics of the procedure in "skull practice," using a blackboard to diagram the position and movement of each individual and team engaged in the procedure. Thought was given to the position of the photographer so that he would not interfere with the smooth performance of the operation.

The only eventuality which was not planned for was the cardiac arrest of the smaller twin. We believe that in some way, before the division of the abnormal major vascular connection between the two, a disproportionate share of the total blood volume was captured by the larger twin.

The single maneuver which gave the greatest comfort and guidance to the surgeon was the preoperative determination of the line of incision by tatooing the skin with methylene blue.

SUMMARY

The successful separation of pygopagous twins is described. Preoperative planning for each eventuality is thought to be a major factor in success. A 33-month follow-up is given.

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Substitute ileal ureter in an infant with congenital hydronephrosis of the left kidney and congenital cystic hypoplasia of the right kidney

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The use of segments of ileum in urinary tract surgery has found wide application since the pioneer work of Bricker[4] with segmental ureteroileostomy. The satisfactory results obtained by Bricker[5, 6] and others[2, 11] with the use of a segment of ileum for a urinary conduit has made possible the partial or total substitution of the ileum for the ureter. The physiologic basis for use of the ileum in the urinary tract has been well founded. The segment of ileum serves as a renal protective mechanism since the active peristalsis prevents stasis and minimizes reabsorption of the urine. Although chloride and urea are absorbed, this has not proved to be a problem clinically.[2, 7] The average amount of the segment fluid emptied at one time with the patient in the supine position is highly constant between 56 and 63 per cent of the total volume.[9]

In 1956, Moore and associates[10] reviewed the background of the use of isolated segments of ileum for ureteral substitution and added their 4 cases to the 20 cases previously reported. Since then, other excellent articles have been published which describe the application for this procedure. The most recent is that of Goodwin, Winter, and Turner[8] in which the authors discussed their 18 cases from the standpoint of indications, results, complications, and function. None of the authors' patients were children. Baum[1] reported the case of a 6-year-old girl with recurrent bilateral hydroureter and left-side infection. The left ureter was reimplanted to bypass a narrowing at the terminal portion of the ureter. The infection recurred. The ureter was then replaced by a 32 cm. segment of ileum. Electrolyte imbalance did not occur up to 1 year postoperatively. The kidney function (phenolsulfonphthalein excretion) improved. The clinical course improved greatly. Thompson[12] reported the first case of total replacement of the ureter in a child with a single kidney. This patient was an 8-year-old male who was admitted with a diagnosis of right hydronephrosis, right nephrostomy, and absence of the left kidney. Bilateral obstructive uropathy had begun at the age of 2 years because of vesical neck obstruction. The left kidney had been removed previously because of pyonephrosis. The right ureter was replaced with an ileal loop. The results of preoperative and postoperative serum electrolyte determinations were within normal limits.

Read at the Annual Meeting of the American Urological Association, Southeastern Section, Jacksonville, Fla., March 14, 1960.
Received for publication Aug. 5, 1960.

With this background and because of our own gratifying experiences with ureteroileostomy,[3] we are reporting in detail the case of a child with congenital cystic hypoplasia of the right kidney and ureter, and hydronephrosis of the left kidney due to left ureteral atresia for which left ureteral replacement was carried out satisfactorily. We believe this to be the second case reported of total replacement of the ureter in a child with one kidney and the first case in which only the one kidney was functioning since birth.

CASE REPORT

R. L., a white male child, was seen 3½ years ago at the age of 3 days because of a large fluctuant mass in the left flank. The urogram showed no excretion of the medium. It was believed that the boy had congenital hydronephrosis which was probably bilateral. His chance of survival was thought to be poor. Surgical intervention was not recommended at that time. He was seen again at the age of 6 weeks and at that time the blood urea nitrogen was 75 mg. per cent, the hemoglobin 8 Gm. per cent, and the carbon dioxide combining power 20 vol. per cent. The quantity of urine was insufficient for testing the specific gravity. It contained 2+ protein. A cystogram with delayed films showed no ureteral reflux. The decision was made to perform a nephrostomy on the left hydronephrotic kidney. The cortex measured only 4 mm. in thickness. A nephrostomy pyeloureterocystogram made 5 days later demonstrated the markedly dilated renal collecting system, a stenotic ureter, and a normal bladder (Fig. 1). The blood urea nitrogen fell to 27 mg. per cent 10 days later. The right flank was explored and a 4 by 5 cm. cystic hypoplastic kidney with no demonstrable ureter was excised (Fig. 2). The pathologist's report stated: "A multilocular cystic structure measures 5.5 cm. in greatest length and 4 cm. in greatest width. The cystic spaces are filled with clear, watery fluid. Sections show the tissue to be composed entirely of cystic spaces which are varied in size and are lined by cuboid and flattened epithelium. There is some associated chronic inflammation and fibrosis but this appears to be a fairly typical case of congenital multicystic disease." At the age of 5 months the child was developing normally. The blood urea nitrogen was 30 mg. per cent. The hemoglobin 11.5 Gm., and the 2-hour PSP showed 25 per cent excretion. The urine showed a maximum specific gravity of 1.012, 3+ protein, and the urine culture showed Aerobacter aerogenes which were resistant to all antibacterial drugs. When the child was 1 year old the blood urea nitrogen was 23 mg. per cent and the urine essentially unchanged except for the urine culture. It now demonstrated Pseudomonas, sensitive only to chloramphenicol. It was decided at this time to attempt reconstruction of the

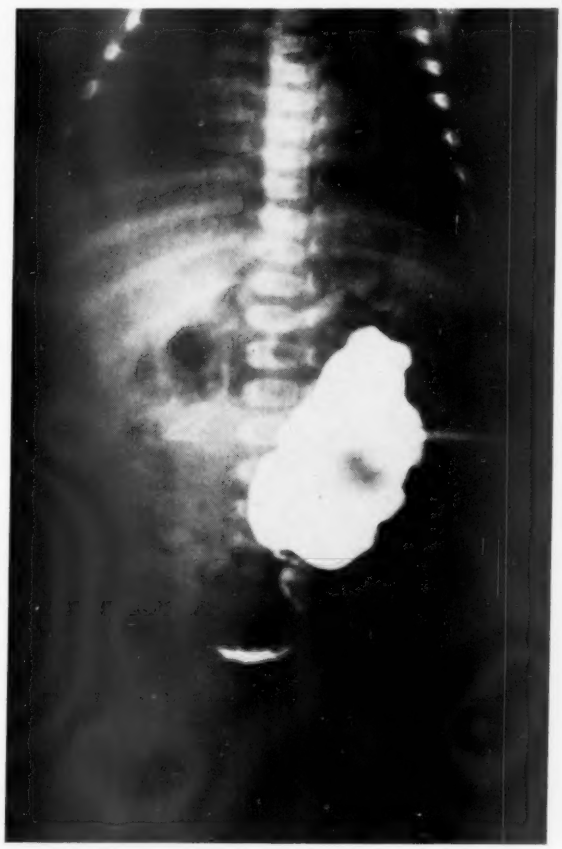

Fig. 1. Nephrostomy pyeloureterocystogram taken when the patient was 7 weeks of age shows a dilated renal pelvis, a stenotic ureter, and a normal urinary bladder.

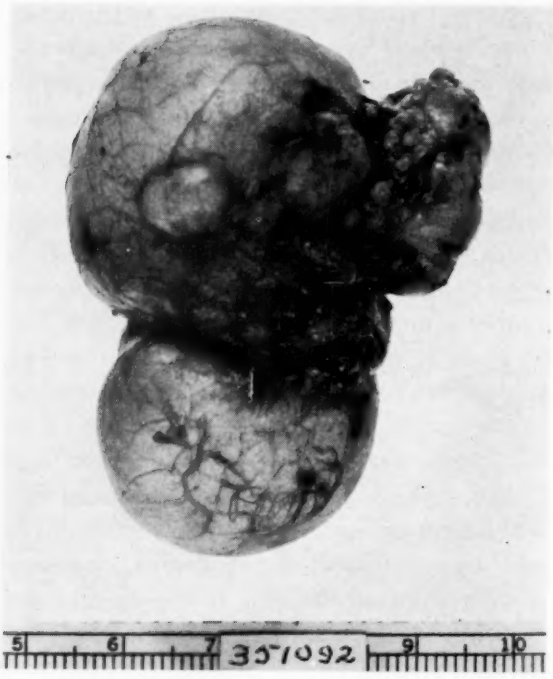

Fig. 2. The 4 by 5 cm. cystic hypoplastic right kidney removed when the child was 7 weeks of age.

Fig. 3. A nephrostomy pyelogram taken when the child was 1 year of age demonstrates that none of the opaque medium entered the ureter.

left ureter. A nephrostomy pyelogram at this time showed that none of the opaque medium entered the ureter (Fig. 3). Exploration of the ureter revealed that it was only a fibrous cord and nothing further was done. When the child was 20 months of age the blood urea nitrogen was 33 mg. per cent and the carbon dioxide combining power ranged from 30 to 54 vol. per cent. It was decided at this time to construct a ureter from an isolated segment of ileum and to maintain nephrostomy drainage until the integrity of the neoureter could be determined.

Operation. The lower abdomen was entered through a left paramedian incision. The left kidney was exposed by incision of the peritoneum lateral to the left colon and reflection of the colon medially. The renal pelvis, which was greatly dilated, was distended with saline through the nephrostomy tube. It was mobilized and its junction with the ureter identified. The stenosed lumen of the ureter would not accommodate a probe from the renal pelvis. The urinary bladder was normal in size and the wall was of normal thickness. A loop of terminal ileum measuring 15 cm. in length was isolated, which reached conveniently from the renal pelvis to the urinary bladder. Care was taken to avoid injury or twisting of the mesentery of this isolated segment. A small incision was then made in the mesocolon of the left colon through which the proximal end of the segment was passed. An ellipse of the lower renal pelvis measuring 2 cm. in length was excised in preparation for anastomosis with the proximal end of the isolated ileal segment. Interrupted sutures of No. 3-0 chromic catgut were used for the inner layer and No. 4-0 silk for the outer layer. The same procedure was carried out in anastomosing the distal end of the ileal segment with the dome of the urinary bladder. The defect in the mesocolon was closed snugly around the ileal segment. Continuity of the ileum was reestablished by an end-to-end double layer anastomosis. The mesentery of the small bowel which formed the ileal segment was

sutured to the posterior peritoneum to obliterate any apertures through which the small bowel could herniate. The segment of ileum used to replace the left ureter lay in good position and was well relaxed with no tension on the mesentery or suture lines (Fig. 4).

The postoperative course was complicated by chicken pox but was otherwise satisfactory. The nephrostomy tube was injected with radiopaque solution with observation by fluoroscopy which demonstrated that the ileal ureter functioned well (Fig. 5). The redundancy of the ileal ureter was intentional since it was uncertain whether the growth in length of the new ureter in subsequent life would be commensurate with the stature lengthening of the torso. The nephrostomy tube was removed 21 days after operation and the sinus tract was dry in less than 12 hours. The urinary bladder functioned well and the patient urinated with a good stream.

At the age of 2 years, 4 months after construction of the ileal ureter, the child was hospitalized with severe metabolic acidosis after a 5-day episode of vomiting and diarrhea. The blood urea nitrogen was 120 mg. per cent and the carbon dioxide combining power was 20 vol. per cent on admission. Adequate hydration and administration of lactate Ringer's solution resulted in a diminution of the blood urea nitrogen to 27 mg. per cent in 5 days and elevation of the carbon dioxide combining power to normal limits. It was the opinion of the pediatric consultant that the patient had prerenal azotemia with metabolic acidosis due to his inability to conserve sodium.

At the age of 3½ years, he appeared and acted normally (Fig. 6). He weighed 22 pounds and was 34 inches in height. The urine had a specific gravity of 1.009 and contained 1+ protein with no pus cells. The blood urea nitrogen was 45 mg. per cent and the carbon dioxide combining power was 30 vol. per cent. The serum sodium was 139.2 mEq. per liter, the serum chloride 114 mEq. per liter, and the serum potassium 4.1 mEq. per liter.

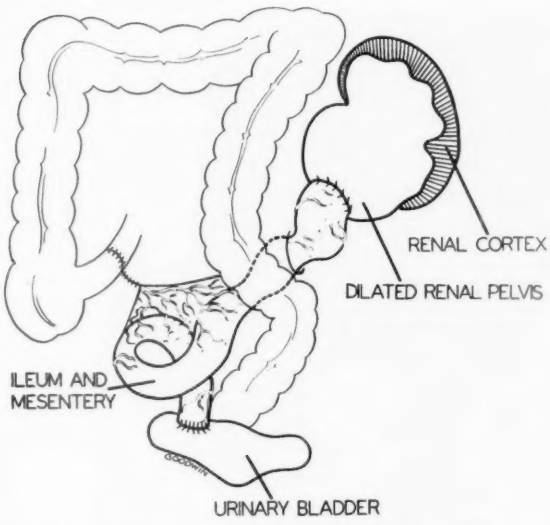

Fig. 4. A diagram which demonstrates the operation performed to replace the left ureter with an ileal segment.

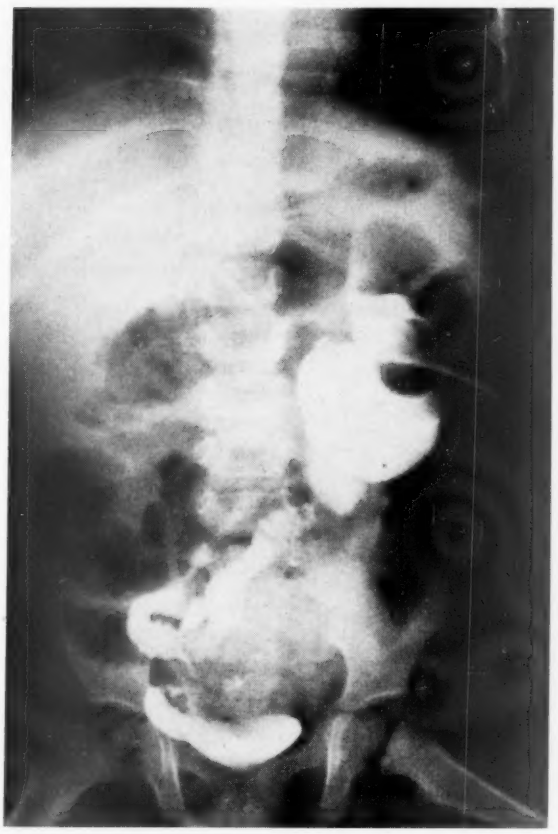

Fig. 5. Injection of opaque medium through the nephrostomy tube before the tube was removed demonstrated that the ileal segment functioned well. The urinary bladder is partially filled.

Fig. 6. The patient at 3½ years of age.

DISCUSSION

The future of this child with his borderline renal insufficiency, is, of course, dependent on avoidance of any renal insult by infection or dehydration by any cause. His parents are well aware of his condition and provide him with an adequate fluid and electrolyte intake. The elimination of the nephrostomy tube and the protective mechanism of the peristaltic action of the ileal ureter should provide him with maximum protection against renal infection. It was encouraging to find no pyuria on his last visit. It is our belief that replacement of the ureter with a segment of ileum is a sound procedure and should find application in cases in which a functioning kidney is present but compromised by an inadequately functioning ureter.

SUMMARY

The case of a child born with congenital cystic hypoplasia of the right kidney and ureter and congenital hydronephrosis of the left kidney is presented. Salvage of the markedly impaired left kidney was accomplished by substitution of an ileal segment for the stenotic left ureter. The case and technique of the operation are discussed in detail. This procedure, by eliminating the nephrostomy tube in the left kidney and adding the protective mechanism of peristalsis to eliminate stasis in the renal pelvis, should give maximum protection to the markedly impaired kidney.

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Appraisal of progress in surgical therapy

Conducted by WARREN H. COLE, M.D.

Cholecystectomy for acute cholecystitis

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Diametrically opposed methods of treatment of acute cholecystitis are employed in various surgical centers. Many surgeons believe that early operation is highly desirable and that delay contributes to increased difficulty of dissection and higher mortality rates. Others believe that the technical dangers involved in this operation, which admittedly often tax the surgeon's ability or lead to inadvertent damage of the common duct, are so gerat that every attempt should be made to delay operation until a more chronic phase of the disease has supervened.

The intention of this paper is not to compare the methods of treatment, but to present a technique that has been found to be satisfactory for cholecystectomy in the presence of acute cholecystitis. Since the technique employed must be far different from that used in the usual cholecystectomy, it is possible that some of the objections to operation in the acute phase would be answered if it were employed.

The procedure necessitates re-emphasis of the method of removal of the gall bladder from above downward, a maneuver which some surgeons maintain is unnecessary, and some say is more hazardous than the usual technique because of increased hemorrhage. On the other hand, I have found this method essential for safe cholecystectomy in difficult cases, and have found little blood loss associated with its use.

Received for publication Aug. 21, 1960.

METHOD

Timing of operation. If the patient has acute cholecystitis without evidence of common duct involvement or pancreatitis, every attempt is made to operate upon him within 4 days of the onset of the attack. Generally, 12 to 24 hours after hospital admission are required for observation, hydration, and preoperative studies. Cholecystostomy is reserved for the very few extremely ill patients who will not tolerate a general anesthesia or who do poorly at the time of operation. It is unnecessary to emphasize the need of an adequate incision, lighting, relaxation, and assistance. In addition, a supply of suction tips of various designs is extremely helpful (Fig. 1).

Incision. If the patient has a broad costal margin or if there is a palpable mass below the margin, a subcostal incision is made. In others a right paramedian incison is used (Fig. 2). It is well to remember that the cystic duct may enter the common duct high under the liver so that the vertical incision usually is better at the crucial spot of the dissection.

Operation. Omentum is freed from the gall bladder. A pericholecystic abscess, if present, is aspirated. The area of the common duct and the pancreas is palpated since the presence of an acute pancreatitis may indicate a more cautious approach than that to be described.

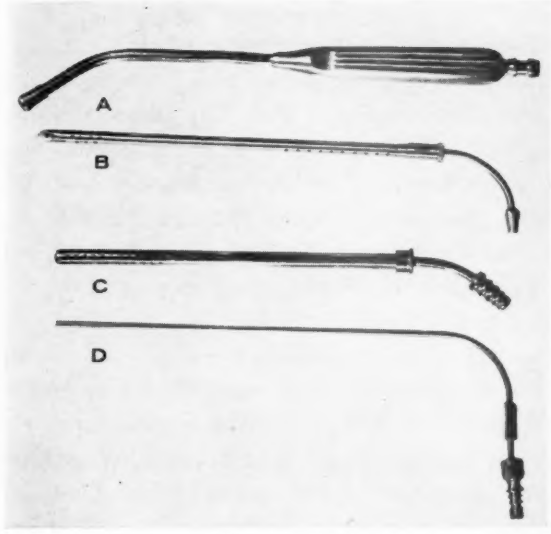


Fig. 1. A, Tonsil-tipped aspirator, *B*, suction trocar, *C*, ordinary suction tip, and *D*, Frazier aspirator.

Aspiration of the gall bladder then is carried out with a suction trocar (Fig. 3). This will facilitate the dissection of the gall bladder from the liver and allow better observation of the common duct area. The aspirated content is observed. If a hydrops is present, a common duct exploration almost surely will not be necessary although if bile is present the possibility of exploration of the duct must be considered.

Next, a brief attempt is made to expose the common duct and cystic duct at the base of the gall bladder. If this is possible, the technique to be described will not be necessary since the usual type of cholecystectomy from below upward may be used. In some instances the probable cystic duct can be isolated and a ligature passed around it. With Glenn's technique, only one loop is set. This will prevent the passage of stones into the common duct with pressure on the gall bladder but does not damage the duct, so that an erroneous ligature can be replaced without hazard. If the anatomy about the base of the gall bladder is at all obscure, the lower dissection is abandoned and the gall bladder is removed from fundus to base.

Dissection from above downward may be quite simple, particularly in the early phase of the disease or if the cystic artery has been thrombosed. In late phases of the cholecystitis, there may be a great deal of vascularity and, unless certain details are followed, the operative field will be obscured by bleeding. If normal saline solution is injected along the upper and posterior walls of the gall bladder the artificial edema created will make separation of the serosa much easier (Fig. 4). It is highly desirable to avoid breaking into the liver bed since, because of the inflammation, it is more hyperemic than normal and control of bleeding may be difficult. During this phase of the dissection the assistant retracts the fundus from the gall-bladder bed, but need not have his hand in the abdomen. Retraction is obtained by an ordinary abdominal wall retractor near the fundus, and a narrow Deaver retractor in the porta hepatis (Fig. 3).

A number of small arteries and veins will be encountered in the bed of the gall bladder during this phase of the dissection. They are divided between clamps and tied immediately. One of the secrets of success in this operation is to avoid the presence of more than 1 or 2 hemostats in the field at one time. Dissection is then carried down the lateral wall, which is the least vascular, and then the medial wall of the gall bladder (Fig. 5).

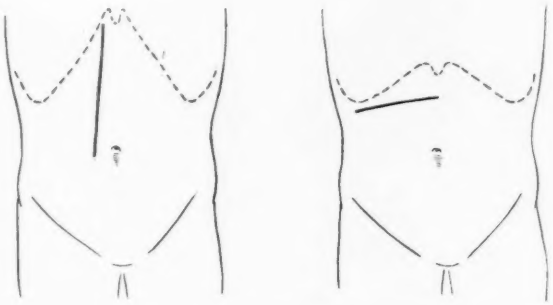


Fig. 2. Incisions. Left, right paramedian, right, transverse.

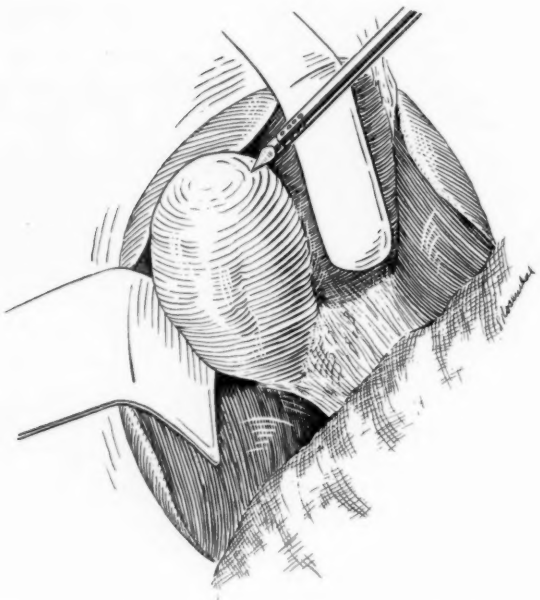


Fig. 3. Aspiration of tense, distended gall bladder.

After the gall bladder has been freed downward for approximately 5 cm., an important change in retraction is made as the ampulla is approached. The assistant now places his left hand in the wound, retracting on both sides of the common duct, so that it is put under tension and straightened out (Fig. 6). Counter-traction is applied by one wide Deaver retractor that is placed over a sponge in the gall-bladder bed and a second narrow Deaver retractor which is retained in the hilum of the liver. At this stage, if there is bleeding, the tonsil-tipped aspirator will dispose of the blood most effectively. At times use of a Frazier aspirator is wise for accurate identification of small vessels or ducts. The usual aspirator is of little value in giving exact exposure at the site of dissection.

At this time the cystic artery is approached for the first time. No attempt will be made to ligate it with one tie. It is exposed at least 1 inch above the presumed junction of cystic and common ducts by

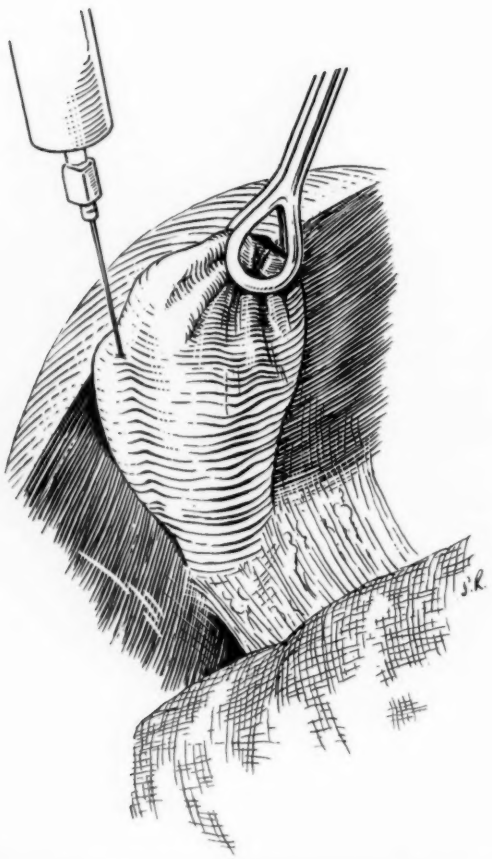


Fig. 4. Injection of saline solution beneath serosa.

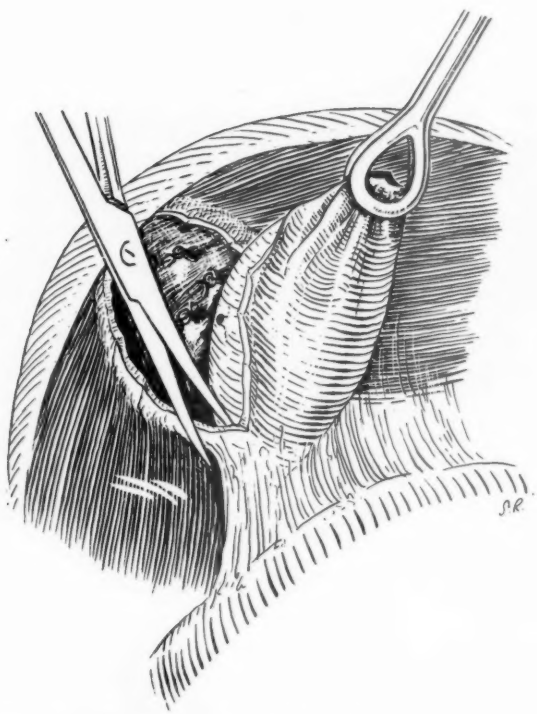


Fig. 5. Gall bladder freed from liver.

cutting through the serosa at this level (Fig. 6). This protection is wise since often the right hepatic artery loops upward on the medial wall of the gall bladder and the cystic artery may be very short (Fig. 7). After the major anterior branch of the cystic artery is tied, it is easy to continue dissection down to the base of the reflection of the serosa from the liver bed. At this point the posterior branch of the cystic artery is clamped and ligated.

The gall bladder then is retracted medially and the peritoneum incised over the lateral margin of the cystic duct (Fig. 7). This area is by far the safest approach to the duct since it is nearly always avascular. The cystic duct may be surprisingly superficial if the ampulla has been greatly distended. The cystic duct can be recognized by its configuration which often persists even with inflammation.

Finally, the medial side of the ampulla and cystic duct are dissected. This will involve the division of several short branches of the cystic artery (Fig. 8). The cystic node is identified and usually removed with the specimen. In many instances the ampulla and cystic duct will be parallel to and be closely opposed to the common duct for a distance of 2 to 3 cm., and this dissection must be carried out with great care. The common duct is identified and the cystic duct junction mobilized. The gall bladder is removed and opened after the cystic duct has been clamped. Usually large stones will be present or stones that are too large to pass through the cystic duct. However, if the gall bladder contains small stones and the cystic duct is dilated, common duct exploration must be considered seriously.

The surgeon often has a delicate decision to make at this time. Realizing that the postoperative course may be complicated if he leaves a stone in the common duct, he must balance this possibility against the dangers and difficulties of a choledochostomy in this particular case. In some instances a dilator may be passed through the cystic duct stump into the common duct and the latter thus may be identified accurately and

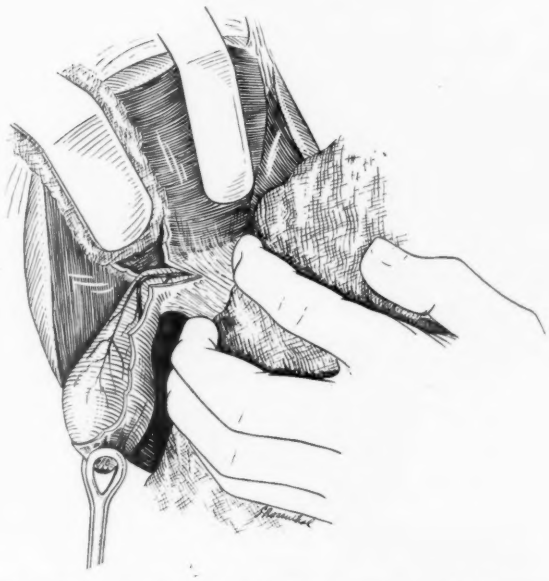


Fig. 6. Ampulla of gall bladder exposed above cystic duct.

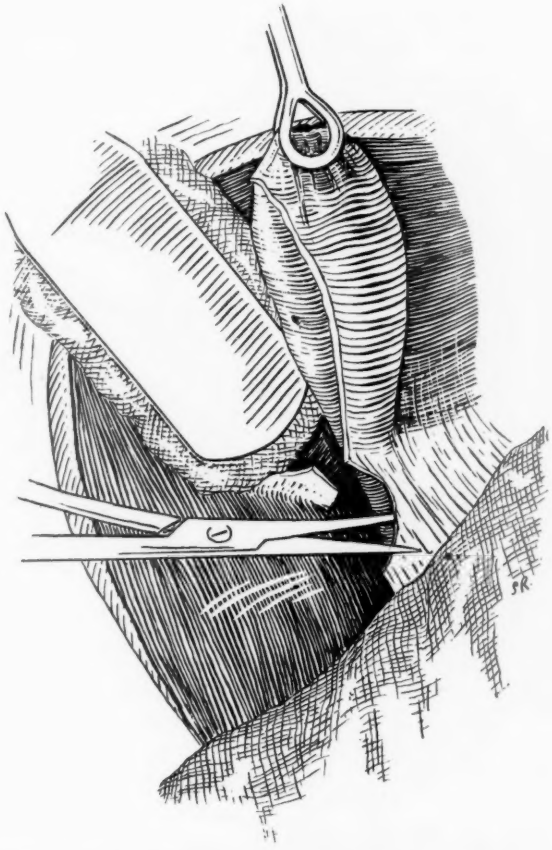
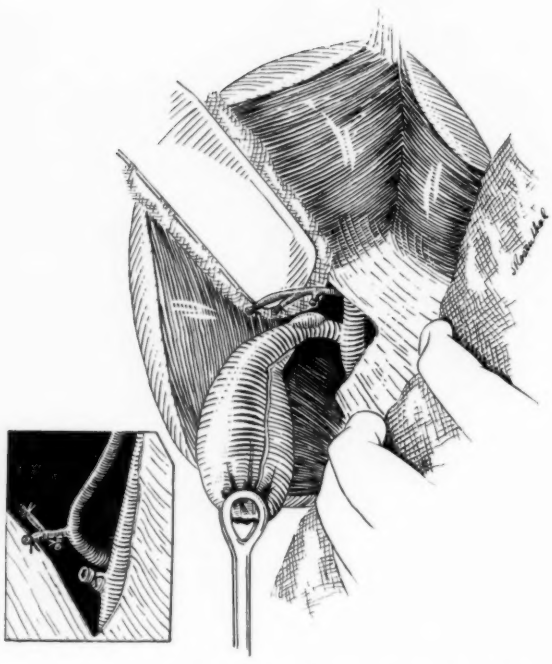


Fig. 7. Mobilization of cystic duct starting on lateral side.



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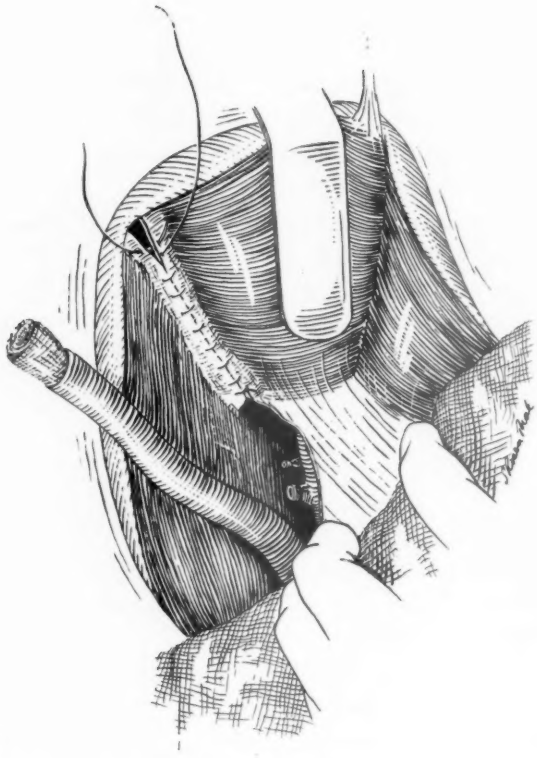

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Fig. 8. Complete exposure of cystic duct. Insert shows a common form of anomalous right hepatic artery with very short cystic artery.

Fig. 9. Closure of gall-bladder bed.

can be opened over the dilator. Common duct exploration through the cystic duct is not a very satisfactory procedure. Operative cholangiograms may well be utilized.

Common duct exploration, because of these increased hazards, has been carried out in approximately 30 per cent of the cases, compared with slightly over 50 per cent in cases of chronic cholecystitis. The method of choledochotomy is not within the scope of this paper.

The cystic duct now is tied securely with catgut about 3 mm. from its junction with the common duct (all previous ligatures have been of cotton). The gall-bladder bed is closed with a running catgut suture. Finally, a cigarette wick is placed in Morison's pouch and brought out through a stab wound. The abdominal wall is closed in layers.

Complications. The most important complication that can occur with this method has been the retention of a common duct stone when the common duct has not been explored. In that case a secondary choledochotomy will be necessary. This has been required 1 to 24 months later in 5 instances. The second most common complication has been brisk bleeding from the liver bed, due either to an inadvertent tear of the capsule or destruction of the capsule by a pericholecystic abscess in the gall-bladder bed. Gelfoam packs have been used occasionally for such bleeding and have proved to be fairly satisfactory, though they contribute to an increased danger of a subhepatic abscess.

In 100 consecutive cases of acute cholecystitis, 99 were treated in this fashion, and 1 by cholecystostomy. There were no deaths in the series. Six secondary common duct explorations have been necessary, including 5 for stones and 1 for a pericholedochal abscess.

Reply to Dr. Casberg on academic tariff

I was greatly disturbed by Dr. Casberg's recent editorial in SURGERY which implies that the American Board of Surgery does not permit foreign medical graduates trained in approved hospitals in this country to sit for its examination. This is a gross and unfortunate error, because the American Board of Surgery in particular makes every effort to assist the foreign medical graduate trained in this country to take these examinations. Indeed, in the present booklet of information a special point is made to encourage the foreign graduate to apply so that his papers may be processed and it will be possible to admit him to the examination promptly on the completion of his residency. We know that many of these men wish to return to their own countries and, therefore, a particular effort is made to enable them to take our examination before leaving.

It may also be of interest that the foreign medical graduate who has received his training in another country may, under certain circumstances, be permitted to take the examination of the American Board of Surgery. It is easy to understand why this can be done only in particular or exceptional instances, but the fact that it is done is another indication of the broad attitude taken by the American Board of Surgery to foreign students. I hope this information will be spread about in Dr. Casberg's immediate vicinity in India.

I cannot speak for other specialty boards in this country, but I can state emphatically that the attitude of the American Board of Surgery is broad, fair, and sympathetic. Indeed, the foreign medical graduate who has his training in this country is allowed to sit for the examination almost without exception. The exceptions relate entirely to poor performance in his residency training program.

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On the treatment of lymphangioma in children

A recent essay on the treatment of lymphangioma in children which appeared in these pages has engendered considerable controversy. A 2-year-old boy was depicted who had been treated for cavernous lymphangioma by forequarter amputation. The illustrations and text overemphasized the concept of radical surgery in the treatment of this disease. Because of the wide audience of this journal among surgeons who are called upon to manage pediatric surgical problems, it should be made clear that the need for such therapy is rare. Indeed, it should be emphasized that the proper management

of lymphangioma does not always demand complete eradication. Rather, repeated local excisions are often to be favored over total ablation of the involved tissue.

Cavernous lymphangioma, however foreboding the nomenclature, is a benign disease. It is not uncommon in the childhood years, yet, strangely, is rarely seen in adults. This form of lymphangioma is disfiguring in certain locations, and by virtue of size or position may occasionally impair function. The tumor insinuates itself in the interstices of muscles, tendons, nerves, and vessels, and thus may impede muscle action, encroach upon the airway, or distort various anatomic units. In such situations prompt surgical excision is necessary. Judged in the light of its integral cellular morphology, however, this growth is as harmless as the sponge which it resembles. It is a misleading inference, therefore, which suggests that the lymphangioma which recurs after excision is a potentially dangerous lesion. In the first place, oncologists are in agreement that cavernous lymphangioma does not undergo malignant transition. Second, it should be appreciated that when lymphangioma is partially excised, the surrounding lymph-bearing tissue frequently increases in size on the basis of redirection of lymph flow and local lymph stasis. Further, if there is true tumor recurrence, repeated local excisions are usually efficacious in producing a result acceptable from cosmetic and functional standpoints. In this regard, the comment by the authors that "such a wound will heal satisfactorily with residual tumor in the margins" emphasizes an important concept in the surgical treatment of lymphangioma.

In view of the established benign character of lymphangioma, surgical treatment should be utilized for the improvement of appearance or the enhancement of function. Thus the statement, "the extent of recurrence required a shoulder girdle amputation" must be challenged. Complete excision of lymphangioma requires a mutilating procedure which compromises function, distorts appearance and, in the absence of malignant threat, serves no purpose. Occasionally, recurrent life-endangering infection or grotesque elephantine appearance may make amputation inescapable, but such treatment is reserved for the exceptional case, and then only after years of conservative measures have failed.

By forequarter amputation a child has been relieved of a benign tumor of the arm and shoulder. He has given his right arm for this treatment. To be sure, the arm had an unsightly soft, spongy thickness, but it could grip a baseball bat, hold a fountain pen, fill a coat sleeve, and extend a firm handshake. Such an arm could, by its presence, declare itself a functioning, growing part of the *whole* child—enhancing the youngster's future without jeopardizing his health. Even if radical extirpation is ultimately necessary, at an age of 2 years no child with lymphangioma has had adequate clinical trial of conservative measures.

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